CARDIAC EMERGENCIES AND HEART FAILURE

Prevention and Treatment

BY

ARTHUR M. MASTER, M.D.

Cardiologist, Mount Sinai Hospital, New York, N.Y., Associate Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University

MARVIN MOSER, M.D.

Assistant Physician in Medicine, Montefiore Hospital, N.Y. Adjunct Physician in Medicine (Cardiology) Grasslands Hospital, Valhalla, N.Y.

AND

HARRY L. JAFFE, M.D.

Assistant Attending Physician, Cardiology, Mount Sinai Hospital, New York, N.Y., Lecturer in Medicine, College of Physicians and Surgeons, Columbia University

Second Edition, Thoroughly Revised

Illustrated



Lea & Febiger

PHILADELPHIA

1955

Library of Congress Card Catalog Number, 55-7847
Printed in The United States of America

PREFACE TO THE SECOND EDITION

During the past three years numerous advances have been made in cardiology and a number of new drugs have been introduced for the treatment of cardiac emergencies. In presenting this revision of the original text, those newer therapies have been stressed which, in our opinion, have proven successful and will continue to be utilized, procedures that appear promising but which have not yet stood the test of time are discussed only briefly. The chapters on congestive failure, arrhythmias, acute coronary disease, rheumatic heart disease and hypertensive crises have been enlarged or revised and case reports added to include newer concepts and to illustrate the use of drugs that have been recently introduced. The bibliography has been brought up to date and the index enlarged. Several charts and tables have been added in the section on arrhythmias. The book has been kept at "pocket size" so that the physician may have it available for use at all times, even at the bedside. As in the first edition, cases have been added from the authors' private practices and from the wards of the Mount Sinai Hospital. We are most grateful to our wives who gave us unceasing assistance in the preparation of this book.

New York, N.Y.

Arthur M. Master
Marvin Moser
Harry L. Jaffe

PREFACE TO THE FIRST EDITION

THE prompt diagnosis of cardiovascular emergencies and their proper treatment are among the most common problems confronting the general practitioner This monograph has been written in the hope that it will be of value to him as he encounters these acute conditions It is not intended to be a book on Cardiology, Radiology or Electrocardiography, consequently, it does not cover these fields as thoroughly as do the standard textbooks Physiology and pathology are discussed when a fuller understanding of them is considered necessary for the intelligent handling of cardiac patients The drugs that have been found valuable are stressed, other drugs in current use are discussed Case histories are presented to illustrate specific conditions and the use of the newer drugs Throughout the book, the importance of preventing cardiac emergencies by adequate interval therapy is emphasized

We have included sections on surgical cardiac emergencies, on cardiac resuscitation and on certain acute conditions that are not commonly encountered, *i e*, dissecting aneurysm, hypertensive crises secondary to pheochromocytoma, and the acute episode resulting from a "ball valve" thrombus, in the hope that when these emergencies are seen they may be recognized and treated properly

The section on congestive heart failure and its complications is brief, but we have included all of the information

that we believe is necessary for the treatment of this condition

We have surveyed the literature, but have drawn freely from our own cases and experience, as well as from material previously published by one of us (A M M). Portions of this monograph have been presented in several broadcasts sponsored by the New York Academy of Medicine over Station WNYC (FM).

We wish to thank Dr. Samuel Kahn and Dr Phillip Samet for editorial assistance We are indebted to members of the cardiographic department of the Mount Sinai Hospital for valuable suggestions

We hope that the great number of physicians who are called upon to diagnose and treat the diseases that we discuss will benefit from this work

New York, N Y

A M M
M M
H L. J

CONTENTS

LIST OF ILLUSTRATIONS

Cardiac Emergencies and Heart Failure

INTRODUCTION

As a result of the tremendous advances in the prevention and treatment of many diseases, and of the increased span of life, cardiovascular disease now greatly outnumbers all others and causes more than half the deaths after the age of fifty Acute heart conditions require emergency treatment more than do those of any other organ, making the term "acute heart" even more appropriate than the expression "acute abdomen" The prompt treatment of acute cardiac disease by the application of well-established rules, and the utilization of recent advances in the field of cardiology will save many lives and hasten recovery in others Since treatment must be immediate, it is incumbent upon the physician to know how to diagnose and treat cardiac emergencies, and to have the essential drugs readily available This requires the careful selection and constant replenishment of medical supplies, for it is very disheartening to make the correct diagnosis of a cardiac emergency, and not to have the suitable medication available The following material should always be present in the doctor's bag in adequate amount Additional drugs, such as intravenous hexamethonium (Chapter 6), which are generally reserved for hospital use, need not be carried but should be available in a hospital.

1 Aminophyllin, ampules, 10 cc. = .24 gm for i v use, 2 cc = .48 gm for i m. use.

2 Atropine Sulfate, .75 mg. (gr. 1/100) hypodermic tablets for i.v. use
3 Cedilanid (Lanatoside C), 4 cc. (.8 mg.) and 2 cc. (.4 mg.) ampules for i.v. or i.m. use.
4. Demerol, 2 cc. (100 mg.) ampules, or multiple dose vials (1 cc = 50 mg.)
5 Digoxin, .25 mg. tablets or Gitaligin, .5 mg. tablets
6 Epinephrine 1:1000 (1 cc. ampules)
7 Isuprel, 10 mg. linguets
8 Mercurial Diuretic (Mercuhydrin or Thiomerin) 1 or 2 cc.
9 Morphine Sulfate, 16 mg. (¼ gr.) tablets for i.m. or i.v. use
10. Needles for phlebotomy
11. Neosynephrin, 1 cc = 10 mg., for i.v. or i.m. use
12 Nitroglycerin hypodermic tablets, gr. 1/200 or gr. 1/150
13 Pronestyl (Procaine Amide), 10 cc. ampules (1 cc. = 100 mg.) and 250 mg. tablets.
14 Quinidine, 1 cc. ampule = .2 gm. for i.m. use, .2 gm. (3 gr.) tablets
15 Sterile water for dilution of tablets.
16 Ouabain (G Strophanthin) 2 cc. ampules = .5 mg., or Strophanthin K ("Strophosid"), 1 cc. ampule = .5 mg.
17 Thorazine, 1 cc. = 25 mg. for i.m. use, 10 or 25 mg. tablets or Dramamine, 50 mg. tablets, 10 cc. ampules (1 cc. = 50 mg.)
18 Tourniquets
19 Vasoxyl, 1 cc. = 25 mg., or Wyamine, 1 cc. = 15 mg. for i.v. or i.m. use

Chapter

1

ARRHYTHMIAS

A CHANGE in the rate or rhythm of the heart is a common cause of acute distress in patients with and without cardiac disease. Even in a patient with a normal heart, an arrhythmia may produce symptoms of anxiety, precordial aching or severe pain,[118] vertigo, syncope, vomiting, collapse, and rarely congestive heart failure.[125] Severe circulatory derangements occur following the onset of arrhythmias with a rapid rate, *i.e.*, the paroxysmal tachycardias, or a slow rate, *i.e.*, complete A–V block. This is especially true in elderly people.

PAROXYSMAL TACHYCARDIA

The paroxysmal tachycardias include atrial flutter and fibrillation, atrial, nodal, and ventricular tachycardia and ventricular fibrillation. (The term "atrial" is to be preferred to "auricular" since the cardiac pacemakers are located in the atrium and not in the appendage (auricle).) Any of the tachycardias may remit spontaneously within several hours and cause no disturbance, but they may produce severe symptoms and marked effects on circulatory dynamics. The clinical severity of any arrhythmia is usually proportional to the increase in the ventricular rate. It has been demonstrated that a change in heart rate from 70 or 80 to one of 120 or 130 usually increases minute volume output. This occurs despite the fact that ventricular filling and stroke volume may be decreased. (The cardiac output,

which is the product of heart rate and stroke output, actually increases.) With further increases in cardiac rate, total minute volume is reduced.[133] This may result in severe cerebral anoxia with fainting or convulsions. For example, J.C., a thirty-two-year-old factory manager studied by us, fainted on several occasions. He gave a long history of discomfort whenever he wore a tie, and his pulse slowed moderately on carotid sinus pressure. The fainting was, therefore, considered to be the result of bradycardia caused by carotid sinus hypersensitivity. Close questioning, however, revealed that the syncope was preceded by palpitations, and he was later seen during an episode of nodal tachycardia. This was probably the major cause of his fainting, although the carotid sinus may also have played a role.

If tachycardia persists, it may result in a further decrease in cardiac output and the clinical picture of shock, cardiac failure,[3,99] and/or coronary insufficiency with chest pain and RS–T and T-wave changes in the electrocardiogram. A patient demonstrating this syndrome was a sixty-five-year-old woman with carcinoma of the left lung and hemothorax who was receiving nitrogen mustard therapy. On the fifth day after therapy she suddenly experienced precordial pain and palpitation and went into shock. Her heart rate was 180, and an electrocardiogram revealed a 2:1 atrial flutter with RS–T depressions in all leads. While the cardiogram was being taken, the rhythm reverted to normal sinus rhythm but the RS–T depressions persisted for several minutes. In some instances RS–T depressions persist for hours or days.

THE SUPRAVENTRICULAR TACHYCARDIAS

Supraventricular tachycardias, i.e., atrial or nodal tachycardia and atrial flutter and fibrillation, occur in persons with normal or abnormal hearts,[43,173] and may be precipi-

tated by emotional disturbances[379] Occasionally, they are the only indication of hyperthyroidism and this disease should be ruled out in all cases of recurrent paroxysmal tachycardia Although the basal metabolic rate is within normal limits in approximately 85 per cent of patients with supraventricular tachycardia,[175] other tests of thyroid function (radioactive iodine [I_{131}] uptake, and blood protein bound iodine) may indicate a hyperthyroid state *Ventricular tachycardia,* on the other hand, is almost always associated with organic heart disease, particularly coronary occlusion,[188] and is of more serious import

In many normal persons with paroxysmal tachycardia therapy may be withheld for several hours since these arrhythmias often remit spontaneously People with normal hearts may be able to tolerate rapid heart rates for weeks or months without exhibiting any detectable alterations in circulatory function[109, 289] Some patients, however, become emotionally disturbed and may experience precordial discomfort as a result of rapid beating of the heart, in such patients, especially those with organic heart disease, treatment should be started immediately Similarly, therapy of the specific tachycardia should not be delayed, even in normal persons, if the patient cannot be observed periodically

Some general measures are of value in the prevention and treatment of all tachycardias, namely, rest, sedation, and the avoidance of tobacco, alcohol, caffeine, and emotional upsets For example a twenty-eight-year-old physician, recently observed, developed atrial fibrillation whenever he took one drink and smoked one cigarette simultaneously He was finally persuaded to stop drinking and smoking and experienced no further attacks Eating fatty foods or large meals on rare occasions produces atrial arrhythmias in patients with otherwise normal hearts We have observed a patient who suffered a bout of atrial tachycardia each time he ate a frankfurter or a large dish of ice cream The

avoidance of these foods completely eliminated the attacks.

ATRIAL FIBRILLATION

Atrial fibrillation is the most common paroxysmal arrhythmia and occurs most frequently in patients with rheumatic *and arteriosclerotic heart disease*[11,173] *but both the paroxysmal* and chronic types are observed in the absence of organic heart disease.[213,237] It may be seen in cases of Graves' disease,[60] *following* operative procedures,[194] in pneumonia and in other febrile illnesses.

Atrial fibrillation has been attributed by some observers to rapid, irregular circus movements initiated in the atrial muscle and perpetuated by the occurrence of local blocks,[196] but this view has been challenged by many authors.[172,173-231,251] These latter investigators believe that *atrial fibrillation is a chaotic disturbance of atrial rhythm in response to stimuli* originating in irritable foci in the atrial muscle and that there is no element of circus movement. According to this opinion, all atrial arrhythmias have a similar mechanism, the only difference between them being the number and frequency of impulses arising from the single focus.[262] This view has not as yet been universally accepted[137] but would appear from the evidence presented to be a logical explanation of atrial arrhythmias.

The paroxysmal form of atrial fibrillation usually sets in abruptly with a ventricular rate between 120 and 160 and a totally irregular rhythm (Table 1). A pulse deficit may be present. The rhythm may revert to normal with rest and the use of sedatives, but if fibrillation persists treatment with either quinidine or digitalis should be initiated, digitalis being given in all cases of atrial fibrillation with cardiac failure. Some observers favor the use of *digitalis*, particularly intravenously, even when congestive failure *is* not present. Although its primary effect in these cases is to slow the ventricular rate, sinus rhythm *is occasionally* in-

Table 1. Clinical Differentiation of Common Supraventricular Arrhythmias

ype of Cardiac Arrhythmia	Rate/Min	Rhythm	Effect of Exercise or Postural Change	Effect of Carotid Sinus Pressure	Chief Diagnostic Features
inus Tachycardia	90–160	Regular	Increases rate	None or temporary slowing	1 Not over 160/min 2 No sudden onset 3 No real effect of carotid sinus pressure
xtrasystoles (premature contractions)	*Usually normal*	*Basically regular*	*May abolish them*	*No effect*	1 Normal rate 2 Extra beats are followed by longer pause than usual 3 Exercise may abolish extrasystoles
aroxysmal Atrial Tachycardia	*160–220* (usually 180–200)	*Regular*	*No effect*	*Returns to normal abruptly*	1 Rate *over 160/min* (usually 180–200) regular 2 Sudden onset and sudden cessation 3 Abrupt return to normal with carotid sinus pressure
trial Fibrillation	Ventricular Rate 120–150 Atrial Rate > 350	Totally irregular	Increases irregularity	No effect	1 Irregularity of rhythm with rapid rate 2 Pulse deficit 3 No effect of carotid sinus pressure 4 Exercise only increases irregularity
trial Flutter	Ventricular Rate 125–180 (2:1 block) Atrial Rate 250–350	Usually regular, may be irregular	May double ventricular rate by temporarily abolishing A-V block	Temporary slowing	1 Rhythm regular or irregular 2 Temporary slowing by carotid sinus pressure 3 Flutter waves in neck

duced following digitalis administration. If *quinidine* is used (Table 2), 3 grains (.2 gm.) should be given orally every two hours. The first dose may be used to test sensitivity since reactions will usually occur within two hours if the patient is allergic to the drug.[183] True sensitivity is unusual however, and treatment of a patient who is critically ill should not be delayed. If there is no change in

Table 2. Suggested Appproach to the Therapy of Paroxysmal Atrial Fibrillation With Quinidine. No Cardiac Failure

		1st Day
1	Rest and sedation	
2	Quinidine	0.2 gm. every 2 hours for 2 doses, *then* 0.4 gm. every 2 hours for 3 to 4 doses. No therapy at night*
		If no response—2nd Day
3	Quinidine	0.4 gm. every two hours for 3 doses, *then* 0.6 gm. every two hours for 3 or 4 doses If no response, quinidine usually will not be effective and patient should be digitalized

*If patient has severe symptoms, quinidine should be continued during night in gradually increasing doses until .6 gm. has been given for 3 doses.

rhythm after four hours, the dose is increased to 6 grains (.4 gm.) every two hours for three or four doses. Occasionally, it is necessary to raise the dose to 9 grains (.6 gm.) every two hours for three or four doses. Quinidine has relatively little cumulative effect and peak plasma levels are reached after 4 or 5 adequate doses have been given.[114] If the same dose is administered thereafter, the plasma level rises only slightly, and it is therefore necessary to increase the dose again to achieve an effect. If quinidine is initially administered every four to six hours peak levels may not be reached for from two to four days. The total daily or

weekly dose is of much less importance in determining plasma concentration than is the amount of the individual dose,[290, 329] as only traces of quinidine are found in the plasma twenty-four hours after the last dose has been given

If regular rhythm is not restored with the dose of 9 grains, larger ones will rarely have the desired effect and the drug should be discontinued Serious reactions (respiratory failure or asystole) may occur if quinidine is given in excessively large doses (over 2½ to 3 gms in a twelve to twenty-four-hour period). Unfortunately there is little correlation between quinidine blood levels and the toxic effects of the drug on the myocardium, so that there is no way of accurately predicting the onset of "toxic effects" Excellent results are occasionally obtained with very small doses It is often best to administer quinidine on a two-hour schedule for five or six doses during the day and omit night medication In this way the patient can be more carefully observed This, of course, should not be done when the patient has severe symptoms and a delay of several hours may be dangerous

We have used quinidine *intramuscularly* during the past four years with good results A suitable preparation is a 20 per cent solution of quinidine sulfate in propylene glycol, 3 grains (2 gm) per cc, although several other preparations are also available The injection is rarely painful,[115] the dosage is the same as when given orally, and toxicity is not increased when the drug is given by this route. Intramuscular medication is especially valuable when oral administration cannot be tolerated in patients who are acutely ill Quinidine hydrochloride is also satisfactory for intramuscular use Intravenous quinidine, which is now available as quinidine lactate, in 10 cc ampules, containing 65 gm, is dangerous and its use must be carefully controlled There is little indication for the intravenous administration of quinidine as most cases in which quinidine will be effective respond to intramuscular or oral medication

If fibrillation persists after a satisfactory trial with quinidine, the patient should be digitalized (*vide infra*). In all recalcitrant cases, it is essential to exclude the presence of hyperthyroidism or active rheumatic fever. In patients with atrial fibrillation and hyperthyroidism the prognosis is excellent, for, once the hyperthyroid state has been corrected,[4] the arrhythmia will disappear in 95 per cent of these cases either spontaneously or following quinidine therapy.

If quinidine restores sinus rhythm, the dose is reduced gradually and a maintenance dose is instituted. Three to six grains (.2 to .4 gm.), three times a day may suffice but in occasional cases 6 to 9 grains (.4 to .6 gm.) four or more times a day may be required for long periods. When quinidine is given four times daily, the first dose is taken early in the morning on awakening, the second at midday, the third in the evening, and the fourth dose just before retiring, in order to maintain adequate blood levels. In unusual instances the last dose must be given during the night.

An example of this type of case is that of a fifty-nine-year-old white male, who had severe rheumatic heart disease and atrial fibrillation and was treated with .3 gm. (5 gr.) of quinidine sulfate orally every two hours, as outlined above. Regular rhythm was restored and he was maintained successfully on .3 gm., four times a day, awakening at 4 A.M. daily for the morning medication. Whenever this dose was omitted, fibrillation recurred.

Three-grain (.2 gm.) enseals of quinidine or quinidine in oil ("Quinidate") are available as "long acting" preparations to avoid giving a dose during the night. The drug in this form is more slowly absorbed, allowing for a greater interval between doses.

If attacks of fibrillation recur infrequently, quinidine need not be maintained more than a week after the acute episode. However, if paroxysms occur frequently, prophylactic quinidine should be continued indefinitely.

Occasionally, the attacks respond to quinidine with increasing difficulty as they become more frequent In such cases it may be more advisable to slow the ventricular rate with digitalis than to attempt to restore sinus rhythm with quinidine A good example of this therapy is presented by a woman of forty-four, who had had rheumatic heart disease with mitral stenosis for twenty years She had developed a cerebral embolus three years ago and since then had experienced frequent atrial premature beats and episodes of atrial fibrillation At first, these readily responded to quinidine but the attacks became very frequent and lasted several days in spite of large doses of this drug The patient was greatly distressed during the attacks and developed great anxiety regarding their recurrence In the next attack digitalis alone was given until the ventricular rate fell to 70 Since then, she has been maintained on 25 mg Digoxin daily, has remained in chronic atrial fibrillation but has been entirely comfortable

Although recent studies have shown that adequate cardiac output can be maintained by many patients with chronic atrial fibrillation if they are adequately digitalized,[169] some of them do better when their rhythm is regular.[34] This is especially true during exercise It has been demonstrated in these patients that cardiac output is increased and venous pressure decreased following conversion to sinus rhythm [140] There is also the ever present danger that thrombi will form in the auricles of the fibrillating heart and that embolization will occur in these patients For these reasons, we believe that an attempt to restore sinus rhythm should be made unless the heart is very large or there is a history of recent congestive failure This opinion is not universally shared, however, and many physicians are satisfied merely to slow the ventricular rate with digitalis It has been repeatedly emphasized in the literature that conversion to sinus rhythm by quinidine may result in embolization or death at the time of the change in rhythm,[210 252] particularly

in patients with mitral stenosis and a large left atrium. This has not been our experience. Although it is often difficult, and occasionally impossible, to restore regular sinus rhythm in these patients, we have not experienced any serious accident during the "attempt."

When employed properly, quinidine is a safe and effective drug. The harmful effects following its use have, we believe, been overemphasized. Several premonitory signs and symptoms of overdosage in patients under quinidine treatment should be kept in mind. The most common of these may be grouped under the term "cinchonism." They include tinnitus, impaired hearing, headache, blurring of vision, giddiness, nausea, vomiting, abdominal cramps, and diarrhea. If the drug is given rapidly, by the intravenous route, respiratory depression and convulsions similar to those seen in animals may result.[117] Rarely, a true idiosyncrasy may be present. In such cases acute respiratory distress and circulatory collapse appear even after small doses. Serious skin eruptions[112] occasionally are a manifestation of quinidine sensitivity and, rarely, thrombocytopenic purpura develops (*vide infra*).[218, 291]

A dramatic instance of quinidine sensitivity was seen in P.K., a teacher of sixty-eight, who had had a coronary occlusion thirteen years ago and who recently experienced ventricular premature beats. On several occasions he developed acute laryngeal edema after receiving 3 grains (.2 gm.) of quinidine twice a day. A single daily dose finally sufficed to prevent the premature beats and no further episode of edema occurred while the patient was on this dose. Another graphic demonstration of quinidine idiosyncrasy was that of S.G., a physician of fifty-six, with essential hypertension and coronary artery disease. On several occasions during the years he had received several grams of quinidine for ventricular premature beats. Six months ago he had taken 3 grains (.2 gm.) of quinidine six times during a two-day period when he developed profuse

ecchymoses in the skin and mucous membranes and profuse hematuria. A blood count showed marked thrombocytopenia. Quinidine was discontinued and recovery occurred spontaneously within three weeks. These sensitivity reactions should be treated by immediate withdrawal of the drug. Blood transfusions should be given if required, ACTH and/or cortisone and antihistaminic preparations may be of great value.

Quinidine produces significant electrocardiographic changes, widening of the QT interval being the most common finding. This is caused by lengthening of the RT segment and, only occasionally, by widening of the QRS complex.[97] The latter indicates a toxic effect of quinidine. These changes were noted in a thirty-four-year-old man who was admitted to the hospital because of recurrent episodes of palpitation and was discovered to have a nodal tachycardia. He was put on quinidine, 6 grains (.4 gm), every two hours. After 8 doses, an electrocardiogram showed a QT interval of .58 seconds, largely as a result of lengthening of the RT segment. When the quinidine was stopped, the QT interval gradually returned to within normal limits within twenty-four hours. The QT interval may be even more prolonged than in the case cited above.' If significant widening of the QT interval is found, or if some of the symptoms listed above become manifest, the drug should be discontinued. If the patient is desperately ill, however, because of an arrhythmia, it may be necessary to continue quinidine administration despite *mild* symptoms of toxicity. Even in these cases, if toxic symptoms increase in severity, the drug should be discontinued and other medication given.

Some authors have stated that quinidine should not be used in the presence of complete atrio-ventricular or bundle branch block,[61] but we have not hesitated to employ it in *supraventricular arrhythmias* with bundle branch block. We have not observed any serious reactions as a consequence of this therapy.

When quinidine is unobtainable, oral potassium (5 to 10 gm daily given in divided doses every four hours) may convert atrial fibrillation to sinus rhythm.[215] This therapy was employed during World War II with excellent results. "Potassium Triplex" provides a palatable liquid preparation.

In the treatment of acute paroxysmal fibrillation, occasional good results with Pronestyl (*vide infra*) have been reported.[167] This drug, however, is not successful in converting chronic fibrillation to regular sinus rhythm, although slowing of the ventricular rate may occur.

If *heart failure* is present during the paroxysm of atrial fibrillation, *digitalis* should be administered immediately. It increases the degree of A-V block and slows the ventricular rate, but usually does not affect the arrhythmia. The measures suggested below (Chapter 2) for the treatment of heart failure should also be instituted. Digitalization can be accomplished in many ways with various preparations. It is advisable to learn the potentialities of one preparation for oral use and of another for intravenous administration.

If the patient is acutely ill and immediate digitalization in indicated, Strophanthin K or Ouabain (G Strophanthin) should be given intravenously. These drugs have a very brief latent period and usually exert an effect in five to fifteen minutes, with a maximum effect in thirty minutes to two hours.[81, 171] A safe initial dose of Strophanthin K is 0.3 mg. and of Ouabain, 0.5 mg. Another 0.1 mg. may be given in half an hour and repeated every hour until the ventricular rate is slowed to 70 or less.[342] The total dose of either drug should not exceed 1.0 mg. in twenty-four hours. Strophanthin K is available in 1 cc. ampules containing 0.5 mg. ("Strophosid") and Ouabain in both 1 cc. ampules containing 0.1 mg. and 2 cc. ampules containing 0.5 mg. We have used both of these drugs intravenously with good results.

Lanatoside C (Cedilanid) may also be given intravenously It has a slightly longer latent period than Strophanthin and causes a decrease in heart rate in from twenty minutes to two hours [82] Its effect lasts longer than that of Strophanthin K or G, making this drug ideal if moderately quick and slightly prolonged action is required The initial dose of 8 mg (4 cc) is approximately one half the digitalizing dose This is followed by 4 mg (2 cc) every four to six hours, as required Cedilanid is available in ampules of 2 cc containing 4 mg and in ampules of 4 cc containing 8 mg

It is important to remember that these preparations are eliminated fairly rapidly, and that the full digitalization effect may be lost if a longer acting digitalis preparation is not administered as soon as practicable, *i e*, within twenty-four hours In this way, digitalization is maintained It is usually not necessary to use intravenous preparations, except in patients with severe heart failure and rapid fibrillation

For oral use, we have found Digoxin, a glycoside of Digitalis lanata, very satisfactory It has the advantage of being a pure substance of definite and constant composition and, unlike digitalis leaf, it is almost completely absorbed from the gastro-intestinal tract [79] It is eliminated rapidly, and is not as apt to cause cumulative toxic effects, such as those produced by more slowly excreted glycosides, *e g*, Digitoxin The effect of a single dose of Digoxin usually persists only for several days,[75] whereas the effect of a full dose of Digitoxin may continue for two to three weeks [71] Digoxin is a safe and effective preparation for oral digitalization (Digoxin may also be used intravenously when a moderately rapid effect is required)

We have recently used Gitalin (Amorphous), a digitalis preparation which is also absorbed rapidly and completely and has a duration of action which is longer than Digoxin and shorter than digitalis leaf or Digitoxin The major ad-

vantage of this compound appears to be the wide margin between the effective therapeutic and the toxic dose.[16,17] With most digitalis preparations the usual therapeutic dose is approximately two-thirds of the toxic one, with Gitalin the amount required for therapy is only approximately one-third of the toxic dose. We have employed this preparation in several patients who developed signs of "overdosage" while on Digoxin and have found that occasionally the use of Gitalin will make it possible to continue digitalization without toxicity. This is not true in all cases.

The amount of any digitalis preparation required for digitalization varies greatly from person to person, and the dosage must be individualized. The effective dose of Digoxin varies between 1 5 and 5 0 mg.[12] An initial dose of 1 0 to 1 5 mg. is given, thereafter, 0 5 mg. is given every six hours, until the desired effect is obtained. The maintenance dose is 25 to 5 mg. (1 to 2 tablets) daily, most patients being well controlled on 25 mg. Frequently, giving 25 mg. and 50 mg. on alternate days proves very satisfactory. If Gitalin is used the patient may be rapidly digitalized by giving 2 5 mg. immediately and 1 0 mg. every six hours. Slow digitalization may be accomplished with this preparation by giving 1 0 mg. every four to six hours, or .5 mg. four times daily until the desired effect is obtained. The average effective dose of Gitalin is 6 0 and 7.5 mg., maintenance is usually achieved with 50 to 75 mg. daily.

Many physicians still use the whole digitalis leaf preparation for both digitalization and maintenance. This preparation is a good one, but the delayed onset of its action and the long period required for its dissipation are often disadvantageous. When the patient will not cooperate and take medication regularly, however, the use of the leaf is preferable, since the effect of Digoxin disappears in forty-eight hours and the patient may go into cardiac failure if he neglects to take it for two or three days. This danger is less when digitalis leaf is used. The whole leaf is much safer

vantage of this compound appears to be the wide margin between the effective therapeutic and the toxic dose.[16, 72] With most digitalis preparations the usual therapeutic dose is approximately two-thirds of the toxic one; with Gitalin the amount required for therapy is only approximately one-third of the toxic dose. We have employed this preparation in several patients who developed signs of "overdosage" while on Digoxin and have found that occasionally the use of Gitalin will make it possible to continue digitalization without toxicity. This is not true in all cases.

The amount of any digitalis preparation required for digitalization varies greatly from person to person, and the dosage must be individualized. The effective dose of Digoxin varies between 1 5 and 5 0 mg.[92] An initial dose of 1 0 to 1 5 mg. is given, thereafter, 0 5 mg. is given every six hours, until the desired effect is obtained. The maintenance dose is .25 to .5 mg. (1 to 2 tablets) daily, most patients being well controlled on .25 mg. Frequently, giving .25 mg. and .50 mg. on alternate days proves very satisfactory. If Gitalin is used the patient may be rapidly digitalized by giving 2 5 mg. immediately and 1 0 mg. every six hours. Slow digitalization may be accomplished with this preparation by giving 1 0 mg. every four to six hours, or .5 mg. four times daily until the desired effect is obtained. The average effective dose of Gitalin is 6 0 and 7 5 mg., maintenance is usually achieved with .50 to .75 mg. daily.

Many physicians still use the whole digitalis leaf preparation for both digitalization and maintenance. This preparation is a good one, but the delayed onset of its action and the long period required for its dissipation are often disadvantageous. When the patient will not cooperate and take medication regularly, however, the use of the leaf is preferable, since the effect of Digoxin disappears in forty-eight hours and the patient may go into cardiac failure if he neglects to take it for two or three days. This danger is less when digitalis leaf is used. The whole leaf is much safer

Fig. 1-5 W. Hypertensive cardiovascular disease. Digitalis toxicity. A—Lead III. 40 ventricular premature beats per 100 beats. B—Lead II. 15 minutes after 10 Gm. Potassium orally. 6 premature beats per 100 beats. C—Lead II. 30 minutes. 8 premature beats per 100 beats. D—Lead II. 45 minutes. No premature beats. (Courtesy of Dr. Charles Kasselberg.)

Table 3. Properties of Digitalis Preparations

	Onset of Action	Duration of Action	Digitalizing Dose	Maintenance Dose	Comments
1 Strophanthin K 2 Ouabain (G. Strophanthin)	Intravenous 5 to 15 minutes Max. effect 30 to 120 minutes	24 to 48 hours	Average 0.5 to 1.0 mg	Not practical	Rapid Digitalisation Occasional severe reaction
3 Lanatoside C	Intravenous 20 to 45 minutes Max. effect 60 to 90 minutes	36 to 72 hours	Average 1.6 mg	0.4 mg i.v. every 4 to 6 hours	Intermediate acting parenteral preparation
4 Digoxin	1 to 2 hours Max. effect 4 to 6 hours	36 to 48 hours	Average 3.5 mg	0.25 to 0.5 mg daily	Relatively safe if toxicity, short duration of symptoms
5 Gitalin (Amorphous)	1 to 2 hours Max. effect approx. 4 to 6 hours	48 hours to 7 days	Average 6.0 to 7.0 mg	0.5 to 0.75 mg daily	Wider margin between therapeutic and toxic dose
6 Digitalis Leaf	1½ to 2 hours Max. effect 6 hours	3 days to 2–3 weeks	1.2 to 2.0 gm	0.1 to 0.15 gm daily	Slow absorption, safe and inexpensive
7 Digitoxin	1 to 2 hours Max. effect 4 to 6 hours	4 days to 2–3 weeks	1.2 to 2.0 mg	0.10 to 0.15 mg daily	High incidence of prolonged toxicity Slow dissipation

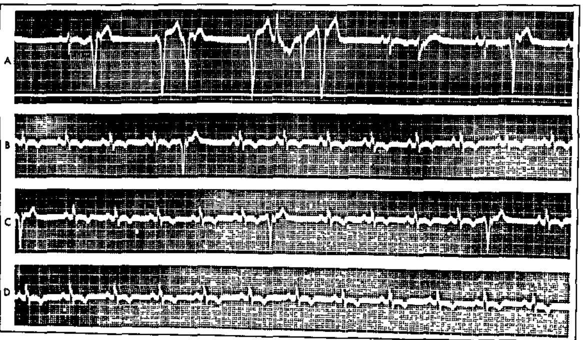


Fig 1-SW Hypertensive cardiovascular disease Digitalis toxicity A–Lead III 40 Ventricular premature beats per 100 beats B–Lead II, 15 minutes after 10 Gm Potassium orally 6 premature beats per 100 beats C–Lead II, 30 minutes, 8 premature beats per 100 beats D–Lead II 45 minutes No premature beats (Courtesy of Dr Charles Enselberg)

arrhythmia except withdrawal of the drug. In some instances of supraventricular tachycardias,[50, 201] ventricular premature beats, or ventricular tachycardias[206] induced by digitalis, specific treatment may become necessary. In these cases, potassium chloride or acetate, given orally, usually eliminates the arrhythmias within thirty minutes[87, 336] (Fig 1) Two to 10 grams of a 20 per cent solution may be given in syrup of citric acid or Karo syrup, or smaller quantities may be given in milk, orange juice, or ginger ale Potassium Triplex (5 cc contains 5 gm each of Potassium Acetate, Potassium Citrate and Potassium Carbonate) is also an excellent way to administer potassium by mouth Five to 10 cc are given in a glass of orange juice as needed When potassium is given in this manner, nausea and vomiting usually do not occur. The effect produced will last only for from two to four hours, and the treatment may have to be repeated Toxic effects of potassium do not occur if there is adequate urinary excretion Rarely is it necessary to use potassium intravenously, if it is, extreme caution should be used, and only 5 to 1 5 gm should be given slowly Electrocardiograms should be taken frequently to detect potassium toxicity Marked peaking of the T-waves, widening of the QRS complexes, and disappearance of P waves are the most commonly observed changes, when potassium intoxication occurs[225]

Recent work clearly demonstrates that potassium depletion may sensitize the myocardium to the toxic effects of digitalis[184] Conversely, maintaining an adequate cellular potassium may actually prevent toxic effects For these reasons we usually give Potassium Triplex (1 teaspoonful, 5 cc, three or four times daily) to patients with myocardial disease in whom digitalis may have to be given in large doses In this way arrhythmias may be prevented.

Atropine is often effective in abolishing the A-V block caused by digitalis

It is often extremely difficult to distinguish between an arrhythmia and symptoms secondary to "overdigitalization" and those resulting from inadequately treated heart failure and "underdigitalization." For example, in patients who are receiving digitalis but remain in severe heart failure with a rapid ventricular rate and nausea and vomiting, it may be impossible to decide whether to withdraw the drug or administer larger doses. A procedure utilizing a rapidly acting digitalis preparation, acetyl-strophanthidin, has been introduced in an effort to determine whether or not a patient is adequately digitalized.[106] Since the effect of this preparation is noted within one to ten minutes after intravenous administration, the status of digitalization may be quickly determined. If a patient is adequately "digitalized" or "overdigitalized," toxic effects will usually appear after the injection of less than 6 mg. of acetyl-strophanthidin. If they do not develop, overdigitalization is not usually the cause of the patient's symptoms or the arrhythmia. This preparation is extremely potent and several fatalities have resulted from its use. We prefer to use either intravenous Lanatoside C (Cedilanid), .4 mg. every three hours, or Strophanthin K, .1 mg. every thirty to forty-five minutes, to determine whether or not a patient is adequately digitalized. Although this method is slower, it is much safer and an answer to the problem is usually obtained within four to six hours.

In atrial fibrillation secondary to hyperthyroidism or active rheumatic fever, digitalis usually does not control the arrhythmia but occasionally has proven effective. For example, a forty-seven-year-old housewife was in severe congestive failure with atrial fibrillation and a ventricular rate of 170 to 180. She was given .8 mg. Cedilanid, intravenously, and .4 mg. intramuscularly four hours later. She also received 2 cc. Mercuhydrin intramuscularly. The next morning atrial fibrillation was still present but her heart rate had slowed to 80 to 90. She had lost 8 pounds and

felt well Radioactive iodine studies later definitely indicated hyperthyroidism to be the cause of her cardiac disability and she responded to treatment with the drug

After the hyperthyroidism has been treated with radioactive iodine, operation or other drugs, the arrhythmia disappears spontaneously or responds to quinidine therapy.[80] A case recently studied illustrates this point A fifty-three-year-old female complained of constant palpitation She had been found to have atrial fibrillation, and had received very large doses of digitalis and quinidine, without abolition of the arrhythmia or slowing of the ventricular rate Although clinical signs of Graves' disease were absent, only 20 per cent of a test dose of radioactive iodine (I_{131}) was excreted and a diagnosis of hyperthyroidism was made A therapeutic dose of 5 millicuries of I_{131} was administered Two days later she was started on 30 drops of Lugol's solution daily This medication was continued for four weeks and, while the fibrillation persisted, the ventricular rate fell to 84 The arrhythmia was still present six weeks after the administration of I_{131} and for this reason 6 grains of oral quinidine were given every three hours Sinus rhythm appeared after 8 doses, and persisted even after quinidine was discontinued

Radioactive iodine is usually picked up by the thyroid gland within twenty-four hours, but its effect on metabolic processes may not become evident for four to six weeks It may be necessary, therefore, as in the case cited, to administer Lugol's solution (10 drops, t i d) during this period This medication may be started twenty-four hours after radioactive iodine has been given and should be continued for approximately three weeks The effect of the Lugol's solution will last for another week, at which time the radioactive I_{131} effect will have begun to manifest itself.

If propyl thiouracil alone is used in hyperthyroid patients, an effect on the arrhythmia should be seen within two to four weeks[7] It should be emphasized that the prognosis in

those cases of atrial fibrillation due to hyperthyroidism is excellent, if the primary disease is controlled.

Cases of atrial fibrillation occurring during active rheumatic fever usually respond to digitalis or quinidine therapy only when the active process has been controlled. Failure to respond to digitalis suggests that the underlying disease is still active. The prognosis in these cases is not nearly as good as in the patients with hyperthyroidism, especially if a mitral valvular lesion is present.[37]

Inability to slow the ventricular rate with digitalis in patients with atrial fibrillation may also be noted in patients with metastatic malignancy involving the pericardium or atrial muscle. In these instances a mechanical factor produces stretching or irritation of the atrium and drug therapy is of no value.

ATRIAL FLUTTER

In *atrial flutter*, the ventricular rhythm is usually regular, with a rate of 125 to 180, but it may be irregular, because of varying degrees of A–V block, and thus may resemble atrial fibrillation. *Atrial flutter may sometimes be distinguished* from fibrillation by the observation of rapid, regular venous pulsations in the neck at a rate over 250, corresponding to the rate of the flutter waves in the electrocardiogram. Usually the atrial rate varies between 250 and 350, and 2:1, A–V block is present, but a marked degree or complete A–V block with very slow ventricular rate may occur. Exercise or position change may temporarily decrease the A–V block and increase the ventricular rate. Carotid sinus pressure does not abolish the flutter but often momentarily slows the ventricular rate.

When atrial flutter is complicated by a bundle branch block pattern, it may simulate ventricular tachycardia electrocardiographically (Fig. 2). Occasionally flutter can be diagnosed with certainty only in the electrocardiographic

leads taken to the right of the sternum,[91] or from the right chest or back In rare instances it is necessary to take esophageal leads to record the atrial waves[52]

Atrial flutter is usually paroxysmal, but it may become chronic and continue for months or years[177] If the paroxysmal type does not remit spontaneously after a short period

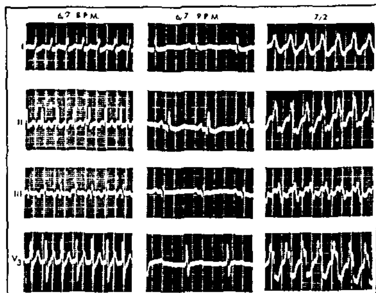


Fig 2—S W, m 71 Atrial flutter treated with intramuscular quinidine, 6 Gm, and oral Digoxin, 8 mg 6/7 8 P M 2:1 atrial flutter 6/7 9 P M 1 hour after therapy, regular sinus rhythm 7/2 2:1 atrial flutter with bundle branch block, simulating ventricular tachycardia

of observation, an attempt should be made to stop the attack with digitalis and/or quinidine (Fig 2) Digitalis is the drug of choice[21,311,341] and is employed in all patients with heart failure Digitalis slows the ventricular rate and increases the efficiency of the heart. It has been repeatedly

stressed, since the original observation in 1911,[191] that digitalis often converts atrial flutter to fibrillation and that sinus rhythm then follows withdrawal of the drug.[141] Although recent observations[33] have cast some doubt upon this theory, we have seen this happen in many patients when digitalis is administered. In some instances digitalis apparently converts atrial flutter directly to sinus rhythm without an *observable* period of fibrillation. In other cases, flutter is converted to fibrillation by digitalis but normal sinus rhythm does not develop when the drug is withdrawn. In these cases quinidine should be administered in an attempt to convert fibrillation to sinus rhythm. Usually a small dose of quinidine is effective.

Digitalis and quinidine are employed as described under atrial fibrillation. In critically ill patients there should be no hesitation about using intravenous digitalis followed by intramuscular quinidine, if necessary. In some instances, atrial flutter persists in spite of all these measures, and the patient must be maintained on digitalis, as in chronic atrial fibrillation, in order to keep the ventricular rate between 65 and 75 beats per minute. Some patients may continue to have atrial flutter for years and then suddenly have the arrythmia remit spontaneously.[204]

If attacks of paroxysmal atrial flutter recur frequently, an attempt should be made to prevent them by the continuous use of quinidine. The dose of quinidine for maintenance is 3 to 6 grains (.2 to .4 gm.), four times a day. In some cases, however, we have found it necessary to increase the dose and the frequency of administration, giving as much as 9 grains (.6 gm.), four or five times a day. If this is not effective, digitalization should be carried out and a maintenance dose continued. In this way a certain degree of A-V block is maintained and, when an attack occurs, the ventricular rate may not markedly increase, despite a rapid atrial rate. This may serve to keep the patient symptom-free during an attack. This method is not

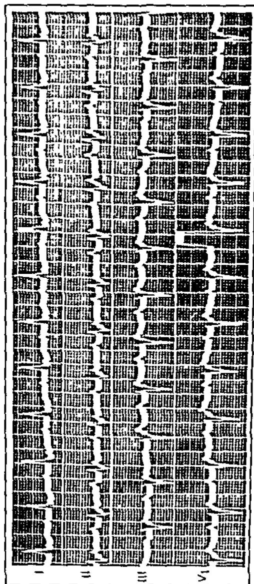


Fig. 3—P E, m 52 Coronary artery disease Paroxysmal atrial tachycardia with 2:1 A-V block. Atrial rate 190, ventricular rate 95

successful in all cases and, despite adequate digitalization, a tachycardia may develop and symptoms appear

ATRIAL AND NODAL TACHYCARDIA

Atrial and nodal tachycardias cannot be distinguished clinically and are treated alike These tachycardias are frequently functional and may be precipitated by tobacco, alcohol, infections, gastric distention, Graves' disease, allergic reactions and tense emotional states Very frequently there is a combination of causes The attack generally begins suddenly although in certain instances there may be a short premonitory period The ventricular rate of 180 to 220 beats per minute usually is regular despite changes of position or exercise,[90] and is somewhat more rapid than in atrial flutter There is usually a 1 1 ventricular response but occasionally a 3 1 or 2.1 response occurs with a resultant ventricular rate between 75 to 100[59] These cases are more common than was previously suspected (Fig 3) Frequently a supraventricular tachycardia can be differentiated from atrial flutter by the absence of flutter waves in the cervical veins Unlike cases of atrial flutter, in which only transient slowing of the ventricular rate may be noted following vagal stimulation, supraventricular tachycardia often is terminated by this procedure These latter arrhythmias are particularly apt to be evanescent, and patients may have many attacks daily for years without experiencing difficulty Patients subject to recurrent attacks have learned, through experience that certain maneuvers stimulating the vagus nerve abolish an attack, e g, sudden movements of the head, holding the breath, coughing, vomiting, eating, lowering the head over the bed, or bending forward in a chair

The attack often disappears spontaneously or following the use of sedatives but, if it persists, an attempt should be made to terminate it by exerting pressure on the carotid

sinus. This maneuver should be tried before other measures are employed. Pressure over the carotid sinus is applied with the patient in the prone position and with the head turned away from the side to be stimulated. The site to be pressed is recognized as a pulsating area at the angle of the jaw, at the level of the thyroid cartilage, here pressure is applied firmly towards the vertebral column. The right carotid sinus is usually more sensitive than the left.[193] Pressure should not be applied on both sides at the same time, especially in old people, and ten to twenty seconds should be the limit for pressure on either side. It should be stopped sooner if slowing of the heart rate occurs. Cases of syncope, convulsions and hemiplegia have been reported following carotid sinus pressure.[41, 315] The prior administration of certain vagotonic drugs, such as Mecholyl[301] or Lanatoside C[129] augments the carotid sinus effect, while Benzedrine, epinephrine, neosynephrin, atropine, or large doses of quinidine may inhibit its effect.[241, 242] If pressure on the carotid sinus fails at first it may be successful later, especially if it is applied in conjunction with one of the drugs which tend to increase its effect. It has been reported that carotid sinus pressure is effective in about 10 to 30 per cent of cases of atrial or nodal tachycardia,[301, 333] although others have had much more success with this method.[186] We have found it effective in about 25 per cent of our cases. Some observers believe that *carotid sinus pressure* or compression is not as effective as actual massage of the carotid sinus and they advocate this procedure.[281] This method of therapy is potentially dangerous in elderly individuals.

Eyeball pressure, when employed properly, stimulates the oculocardiac reflex and produces inhibitory effects upon atrial muscle and atrio-ventricular conduction.[187] Pressure for twenty or thirty seconds is applied over both eyeballs simultaneously, the fingers pressing on the closed eyes just below the supraorbital ridge, and not over the cornea.

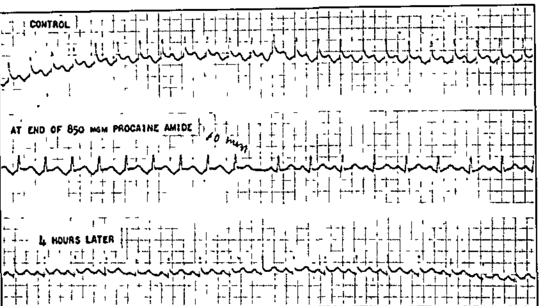


Fig 4—M B, m 45 Paroxysmal nodal tachycardia of unknown etiology Cessation 10 min following 850 gm procaine amide intravenously Continuous lead II (Kayden Steele Mark and Brodie, Courtesy of Circulation)

Occasionally, a patient responds to eyeball pressure but not to carotid sinus stimulation The danger of retinal detachment occurring in myopic individuals following this procedure has recently been stressed [282]

If the tachycardia persists despite these measures, quinidine, digitalis or procaine amide (Pronestyl)[221] should be used Some authors prefer to employ digitalis routinely and it should, of course, be used in all cases of supraventricular tachycardia complicated by congestive heart failure, full *digitalization* is accomplished rapidly by mouth or vein as in atrial fibrillation or flutter This drug appears to be most effective in the treatment of these tachycardias when given by the intravenous route For example, excellent results have been obtained within ten to thirty minutes, with 1.2 mg of Lanatoside C (Cedilanid) [14] *Quinidine* may be given orally or intramuscularly as previously outlined. It is effective in supraventricular arrhythmias in approximately 60 to 80 per cent of cases *Pronestyl*, with an action similar to that of quinidine, is also effective in a large percentage of cases of atrial or nodal tachycardia Figure 4 shows the rapid effect of .8 gm of the drug given intravenously to a man with nodal tachycardia This patient of forty-five developed repeated episodes of this arrhythmia but no cardiac disease could be demonstrated.

Pronestyl is considered the drug of choice in atrial and nodal tachycardia by some observers[24] if carotid sinus pressure fails Our own experience indicates that this drug offers few advantages over quinidine in supraventricular arrhythmias but occasionally is effective when the latter drug fails This is illustrated by the case of a sixty-seven-year-old female with arteriosclerotic heart disease and repeated episodes of paroxysmal supraventricular (nodal) tachycardia who was admitted to the hospital with nodal tachycardia and a ventricular rate of 150. Sedatives, carotid sinus pressure and .6 gm of quinidine given over a period of 4 hours did not effect the arrhythmia. The next

morning intraventricular block was noted, although it was probably the result of the persistent rapid ventricular rate, it was considered best not to continue quinidine 250 mg of Pronestyl were given intravenously and regular sinus rhythm was restored The ventricular rate slowed to 85 to 90 and the intraventricular block disappeared promptly The patient made an uneventful recovery

Pronestyl may be given orally (250 to 500 mg every four hours), intramuscularly (as the hydrochloride) or intravenously (slowly with electrocardiographic and blood pressure control) Details of its administration are noted below

In cases in which mechanical methods are unsuccessful, and in which more rapid action than is usually provided by quinidine is desired, *neosynephrine* may be employed When given intravenously, in doses of 5 mg, this drug usually stops an attack of supraventricular tachycardia within twenty to thirty seconds [144] It produces a rise in blood pressure, stimulation of the cardio-inhibitor fibers in the aortic arch and carotid body, and reflex cardiac slowing [171] Most attacks revert when the systolic blood pressure has risen to 160 mm and the pressure usually returns to normal within ten minutes or less There are few toxic effects of the drug but it should not be used in patients whose blood pressure is elevated during an attack or in cases with ventricular premature beats We have found neosynephrine effective in several cases after all other methods had failed Other pressor drugs such as Vasoxyl may also be used in treating supraventricular tachycardia

If the above physical measures and drugs do not stop the tachycardia, vagal reflexes may be stimulated by inducing vomiting with syrup of ipecac, 4 to 8 cc by mouth [230] The dose may be repeated in forty-five minutes and larger doses may be given if necessary This drug is highly successful in stopping an attack of tachycardia, but its unpleasant effects, *i e*, severe nausea and vomiting, have

limited its use and *we do not employ it unless absolutely necessary*

Mecholyl (Acetyl beta methylcholine) is usually effective in treating supraventricular tachycardia, and restores normal rhythm within a few minutes,[103] but this drug, too, may produce serious and annoying side effects, and consequently *we do not use it, unless other measures fail* It is injected subcutaneously, the initial dose being 20 milligrams This may be repeated in twenty to thirty minutes The effect of Mecholyl may be enhanced by massaging the site of injection and pressing the carotid sinus. The drug may cause severe nausea, vomiting, diarrhea, salivation, precordial pain or occasionally collapse. Shock and death[1] have been reported following its use Therefore, it is absolutely essential that atropine sulphate, 1 to 2 mg (gr 1/60 or gr 1/30) be on hand when Mecholyl is used, since it relieves these symptoms immediately when given by vein. Mecholyl should not be given to allergic or asthmatic patients because of the danger of inducing bronchial spasm, or to hyperthyroid patients because atrial fibrillation may be precipitated[240] It is best to keep the patient in a horizontal position when this drug is used to avoid possible syncope Mecholyl and carotid sinus pressure usually are ineffective in cases of atrial tachycardia with A-V block and in atrial flutter and fibrillation, and they may be ineffective if quinidine has been administered previously[301]

A less toxic parasympathomimetic drug which is effective in the treatment of supraventricular tachycardias is acetylcholine[1] The effect of this drug is brief, and its side effects are less marked than those of Mecholyl Although we have had little experience with this preparation, other observers[1] have found it to be satisfactory when given in a single intravenous dose up to 100 mg

Neostigmine, another parasympathomimetic drug, is also effective in abolishing supraventricular tachycardias and is given in doses of 1 mg intramuscularly[321] When any of

Table 4. *Differential Diagnosis and Treatment of Paroxysmal Tachycardia*

Type of Arrhythmia	Other Diseases Present	Signs Heart Rate—Pulse Rate Symptoms	Electrocardiogram	Treatment*
(A) Acute Paroxysmal Atrial Fibrillation	(1) Rheumatic hypertensive or arteriosclerotic heart disease (2) Common in normals (3) Graves disease (4) Infectious postoperative etc	Heart rate 120-180, pulse deficit may be present Pulse rate 70-120 or more, completely irregular Occasional syncope	No P waves completely irregular rhythm	(1) Sedation (2) Quinidine (3) Digitalis (4) Pronestyl
(B) Atrial Flutter	(1) Most common in rheumatic and arteriosclerotic heart disease (2) May occur in normals	Pulse rate 125-180 depending on degree of heart block, rate varies as degree of block changes Flutter waves in neck at rate of 230-300	Flutter waves at rate of 230-350 Regular or variable rhythm	(1) Digitalis until fibrillation then stop, or continue to keep slow rate (2) Quinidine (3) Pronestyl
(C) Supraventricular Tachycardia (a) Atrial Tachycardia (b) Nodal Tachycardia	(1) Patients usually normal unstable individuals (2) In organic heart disease (3) Postoperative (4) Graves disease	Palpitations dizziness and precordial pain may occur Rate 140-220	Absolutely regular rhythm P waves present Short P-R interval or P waves may occur after QRS complex	(1) Sedation (2) Vagal stimulation by carotid sinus pressure, etc (3) Drugs Neosynephrine, digitalis or quinidine If no effect, Mecholyl Acetylcholine etc
(D) Ventricular Tachycardia	(1) Usually patients with or after coronary occlusion (2) Digitalis intoxication (3) Heart failure	Occasional syncope Pulse rate 150-250 Blood pressure low to shock level Variation of intensity of first heart sound Rarely prominent neck pulsations	QRS abnormal and widened Rate *slightly irregular*	(1) Pronestyl, i v , i m or by mouth (2) Quinidine, i m , or by mouth
(E) Ventricular Fibrillation	(1) Usually patients with arteriosclerotic heart disease	Stokes - Adams seizures common Pulse unobtainable Heart rate not obtainable Blood pressure—shock levels	Extreme, bizarre QRS complexes	(1) i v Quinidine—not to be used *in complete heart block* (2) i v Pronestyl *not to be used in complete heart block* (3) i v $MgSO_4$ (4) i v Atropine

* See text for complete details

these drugs is used atropine should be available for immediate use.

It should be remembered that supraventricular tachycardias so often remit spontaneously that the accurate appraisal of the efficacy of any drug in their treatment is difficult If there are numerous recurrences of the tachycardia, the frequency of the attacks may be diminished by the continued use of quinidine, Pronestyl or digitalis.

A review of the common clinical features of the supraventricular arrhythmias is presented in Table 4

VENTRICULAR TACHYCARDIA

Ventricular tachycardia is infrequent and is usually associated with severe coronary artery disease and coronary occlusion It may be seen in cases of rheumatic heart disease, during cardiac catheterization or operation, and occasionally in normal persons [5] Its occurrence in patients with the Wolff-Parkinson-White syndrome is not uncommon Occasionally it is possible to differentiate ventricular tachycardia clinically from atrial tachycardia by a slight irregularity in rhythm and a variation in the intensity of the first heart sound The cardiac rate should be counted over a period of two or three consecutive minutes. If the rhythm is basically regular at a rate of 150 to 250 but there is a rate variation (3 to 10 beats) from minute to minute the tachycardia is probably ventricular rather than atrial or nodal. Prominent jugular vein pulsations, representing a summation of the atrial systolic wave (A wave) and the ventricular systolic wave (C wave) may be observed at a rate slower than that at the apex, although this is not a common finding

Digitalis is often a factor in the production of ventricular tachycardia [335] Some observers believe that all cases of the bidirectional type of this arrhythmia are secondary to digitalis overdosage.[199] We have stressed the fact that digitalis

should be discontinued in all patients who develop ventricular premature beats, especially if they are multifocal. If this precaution is taken, many cases of ventricular tachycardia can be prevented.

Ventricular tachycardia usually responds to quinidine or Pronestyl. *Quinidine* may be given orally or intramuscularly; occasionally, an intravenous dose, (1 gm., 15 grains) has been required to stop an attack.[22] We believe, however, that quinidine should be used intravenously only if absolutely necessary because of its toxicity when given by this route, and because intravenous Pronestyl is safer if an immediate effect is required.

Pronestyl, a procaine derivative, is very effective in the treatment of ventricular tachycardia.[204] It is a direct myocardial depressant with an action similar to that of quinidine. Pronestyl is supplied in 250 mg. capsules for oral use, and in ampules containing 100 mg. per cc. for intravenous administration. We have used it with excellent results in ventricular tachycardia and premature beats, including cases in which quinidine has failed. It is given orally in doses of 500 mg. every three to four hours, or intravenously in doses of 250 mg. to 1 gm. at a rate of 100 mg. per minute every thirty to sixty minutes until an effect is obtained. An electrocardiogram should be taken while Pronestyl is being given intravenously as it is often effective immediately. If a change in rhythm or widening of the QRS complex occurs, the drug should be stopped. Occasionally oral doses up to 6 or 10 gm. are required. We have found that both routes of administration are satisfactory for the treatment of the acute episodes but intravenous administration produces a much more rapid effect. Ventricular tachycardia may be converted to regular sinus rhythm in from thirty seconds to two minutes following as small a dose as 250 mg. of Pronestyl. A case recently observed is of interest to illustrate the effect of this drug.

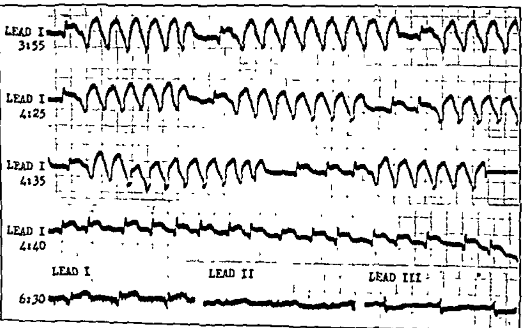


Fig 5—M Y, m 68 Acute coronary occlusion Precordial pain, heart failure and occasional palpitation 10 days Strophanthin K 4 mg just prior to admission Pronestyl 1 0 gm orally 3 45 P.M. Digitoxin 1 0 mg orally at 8 P.M.

A sixty-six-year-old white male experienced an attack of squeezing, severe chest pain radiating to the left shoulder and arm ten days prior to hospital admission Four days prior to admission he developed dyspnea, on the day of admission he became dizzy and weak, noted palpitations, and fainted On admission, he was in acute pulmonary edema and was given 4 mg Strophanthin K intravenously, morphine, and 2 cc Mercuhydrin intramuscularly The electrocardiogram showed runs of ventricular tachycardia and acute anterior wall infarction (Fig 5) He was given 1 gm. of Pronestyl by mouth and normal sinus rhythm developed within an hour (Fig 5) The Pronestyl was continued in doses of 1 gm every four hours for two days, and then in doses of 5 gm every four hours for eight days He was also digitalized with Digoxin and made an uneventful recovery

Pronestyl generally does not produce serious reactions, but when administered intravenously it may cause a marked fall in blood pressure or even cardiac standstill The injection should be given slowly and blood pressure readings should be made during the injection If a fall in blood pressure does occur, it may be counteracted by Neosynephrin (1 to 5 mg) intramuscularly (25 mg Neosynephrin may be given prophylactically with the Pronestyl) When given orally in large doses Pronestyl may produce nausea and other gastric symptoms making it necessary to stop therapy or reduce the dose Fever, chills, malaise and skin rashes have also been noted following its use* We have observed one patient who developed agranulocytosis while receiving Pronestyl and this has recently been pointed out by others Frequent blood counts should be taken and evidence of purpura or bleeding watched for

Pronestyl is occasionally useful in the prevention and treatment of ventricular arrhythmias associated with operative procedures[184] although some observers doubt its effectiveness If used preoperatively, 1 to 2 gms may be given

by mouth forty-five to sixty minutes prior to surgery, and 1 gm given intravenously as the operation is begun. During anesthesia and operation, intravenous procaine may be used instead in a dose of 5 cc of a 1 to 2 per cent solution, to prevent ventricular arrhythmias [49]

Pronestyl has now been used prophylactically by us in a small series of patients who had previously experienced repeated bouts of ventricular tachycardia Although it terminates the acute attack effectively, it does not appear to be completely effective in preventing recurrence of attacks when used orally, 500 mg, 3 to 4 times daily It may be that this dose is inadequate, and patients with repeated attacks may require much larger doses. At the present time the best procedure appears to be to give Pronestyl for the acute episode and quinidine prophylactically

Many other drugs that have been used in the treatment of ventricular tachycardias deserve mention at this time One of these agents, intravenous magnesium sulfate, is not widely used, but has proven effective in occasional cases [39] When given rapidly, in 2 to 4 gm doses, i e, 10 to 20 cc of a 20 per cent solution, this drug may terminate an attack after other measures have failed Transient, unpleasant side effects such as nausea, flushing, weakness, and dizziness may appear It should be reserved for use after other therapy has proven ineffective. With the new agents available, little opportunity for the use of magnesium sulfate presents itself Atabrine, in doses of .4 gram intramuscularly, may occasionally be effective [113] Intravenous morphine sulfate, 10 to 20 mg (1/6 to 1/3 gr), repeated every hour if necessary, has also been used successfully by several observers [122 140]

The use of potassium salts (citrate or acetate in syrup or water, or chloride as enteric coated tablets) orally, either alone in doses of 1 to 5 gms two to four times daily, or in conjunction with quinidine, has been advocated for the

treatment of refractory cases, or to diminish the frequency of recurrences of ventricular tachycardia.[107] We have found potassium to be particularly useful in the treatment of ventricular tachycardia secondary to digitalis overdosage and in patients who are sensitive to quinidine. Dibenamine hydrochloride, Dibenzyline and Regitine, specific adrenergic *blocking agents, have been shown to be effective in* blocking arrhythmias which occur during cyclopropane anesthesia,[161, 245] but we have not used them in the treatment of tachycardias.

VENTRICULAR FIBRILLATION

Ventricular fibrillation is rarely diagnosed clinically, and, although it probably accounts for some cases of sudden death, it is difficult to state its exact incidence. Many Stokes-Adams attacks are the result of ventricular fibrillation, in fact, this arrhythmia is frequently noted in patients with varying degrees of atrioventricular block. Most episodes of ventricular fibrillation occur in association with myocardial infarction, anesthesia, electric shock or excessive amounts of digitalis, quinidine, Pronestyl or other myocardial depressants or stimulants. The patient becomes pulseless, unconscious and rapidly goes into shock. Convulsions may occur if this arrhythmia persists for more than thirty seconds. The electrocardiogram shows bizarre ventricular complexes and a completely irregular rhythm. *Clinically,* these attacks resemble a Stokes-Adams seizure secondary to complete heart block and cardiac standstill and *it is important to distinguish between these conditions* electrocardiographically. The use of sympathomimetic drugs such as epinephrine or ephedrine, which are so valuable in the treatment of cardiac asystole, is contraindicated in *ventricular fibrillation. If possible, the physician should obtain* an electrocardiogram during the attack to establish its exact mechanism. Once an episode is diagnosed correctly

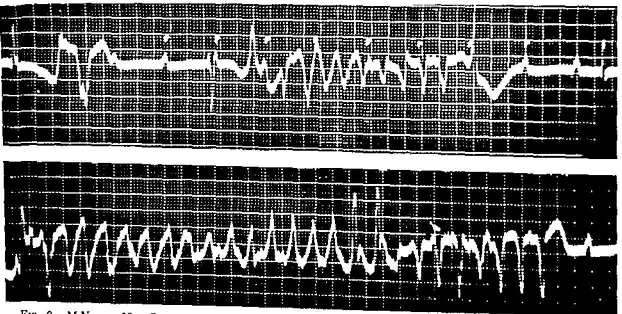


Fig 6—M N., m 60 Coronary artery disease Complete A–V block with periods of ventricular fibrillation and Stokes-Adams seizures Lead II continuous

as ventricular fibrillation, it can be assumed that subsequent attacks will be caused by a similar mechanism and not by cardiac standstill, and they may be treated accordingly. Unfortunately this is not always the case as bouts of both ventricular fibrillation and cardiac asystole may occur in the same patient (Fig 6)

The treatment of ventricular fibrillation during operative procedures is discussed in detail in Chapter 9. Treatment of this arrhythmia when it occurs secondary to other factors is by no means standardized Oxygen should be administered immediately and intravenous procaine given If this is not available either procaine amide (Pronestyl) (100 mg/minute) or quinidine (4 to 6 gm) is given intravenously, despite the fact that this route of administration is not without danger If either drug is given carefully with *electrocardiographic control, an occasional good result may* be obtained *Neither drug should be used in patients with previous, known complete heart block* Pronestyl is probably the safer drug The cautious administration of intravenous magnesium sulfate (10 cc. of a 20 per cent solution) or potassium chloride is also occasionally satisfactory. Intravenous atropine, 2 mg (gr 1/30), has been used successfully to abort the acute attack, and smaller doses, 5 mg (gr 1/100), intramuscularly have been given daily to prevent recurrent bouts in patients subject to paroxysmal ventricular fibrillation[287] In many cases the attack will cease or the patient expire before therapy can be instituted.

HEART BLOCK

Complete heart block, with sudden failure of the idioventricular pacemaker and asystole, is the most common cause of Stokes-Adams syndrome although a similar clinical picture may be seen in cases of ventricular tachycardia or other arrhythmias[271] Heart block is usually seen in patients with organic heart disease secondary to coronary arterio-

sclerosis, but a small percentage of cases results from digitalis overdosage Many patients experience only momentary weakness or unconsciousness and require no therapy, but others have severe symptoms and require immediate treatment

If asystole is established as the cause of an episode of unconsciousness, vigorous thumping on the precordium may immediately restore cardiac action This simple procedure has proved effective in many instances[25,268] If this does not produce a satisfactory result, one-half of one cc of a 1 1000 solution of epinephrine may be given intravenously, or directly into the heart, in extreme cases in shock. If the seizures recur, the Adrenalin should be repeated subcutaneously every hour or two, or may be given in oil (1 cc = 2 mg) intramuscularly, every twelve to twenty-four hours We have observed a fifty-six-year-old female who required 5 cc of Adrenalin every fifteen to thirty minutes for hours, in order to remain free of attacks Intracardiac Adrenalin was necessary on one occasion after intramuscular therapy had failed, and during a period when the patient experienced recurrent Stokes-Adams seizures, a slow, continuous intravenous injection of 1 100,000 Adrenalin at a rate of 2 0 cc (30 drops) per minute was maintained for several hours in order to stop the syncopal episodes In using epinephrine for the treatment of asystole, care should be taken not to administer it too rapidly since ventricular tachycardia or fibrillation may result following relief of the asystolic phase In patients who experience frequent episodes of Stokes-Adams seizures, ephedrine gr 3/8 to 3/4 (25 to 45 mg) or Paredrine gr 1/3 to 1 0 (20 to 60 mg) may be given orally three to five times daily in an effort to decrease the number of recurrences[243] Sublingual *Isuprel* (10 to 15 mg every four to six hours) has been of value in many cases In all cases where digitalis may be a contributing factor this drug should, of course, be withdrawn.

Some observers have achieved results in the treatment

of patients with complete heart block and ventricular standstill by the use of an externally applied cardiac *pacemaker*[346] The pacemaker is not effective in treating syncopal attacks due to paroxysmal ventricular tachycardia or fibrillation

OTHER ARRHYTHMIAS

Sinus bradycardia, sinus tachycardia and premature beats may occasionally cause severe difficulty These will be discussed briefly

Sinus tachycardia is usually associated with febrile or toxic conditions, congestive heart failure, or emotional or metabolic disturbances There is no specific therapy other than that directed at the primary condition This should be carefully searched for and treated Occasionally dramatic results may be obtained For example a seventy-year-old woman who had experienced almost nightly episodes of persistent sinus tachycardia (rate 130 to 150) had been treated for one year with intravenous sedatives and Demerol during each attack Severe angina occurred and the patient was almost a total invalid It was demonstrated that each bout of tachycardia was closely related to painful bowel movements associated with large hemorrhoids and that the resting pulse rate of 100 to 110 in between attacks was most probably the result of hyperthyroidism (radioactive I_{131} uptake of 57 per cent) Following therapy with propylthiouracil and removal of the hemorrhoids, all attacks ceased, angina completely disappeared, and the patient did remarkably well

Sinus bradycardia, like sinus tachycardia, may be an incidental finding, especially in athletes and pregnant women, and usually requires no treatment It is caused by an increase in vagal tone, or by a diminution in sympathetic tone, or both[103] If the rate falls below 40, dizziness and syncope may result, as in a person with carotid sinus syn-

drome. Actual cardiac standstill may occur.[255] We recently observed a basketball coach of thirty-two who usually had a pulse rate of 48 beats per minute. He fainted on several occasions during tense moments in a game During the attacks of syncope his pulse rate fell to 30, but he usually recovered after thirty to forty seconds Usually these cases respond to ephedrine in 25 to 45 mg (⅜ or ¾ gr.) doses, or to atropine sulphate (.4 to .6 mg) gr 1/150 to gr 1/100 by mouth It may be necessary to give atropine (6 mg to 2 mg) gr 1/100 to 1/30 subcutaneously or intravenously, if an immediate effect is desired

Premature beats may cause palpitations, precordial discomfort and anxiety, particularly if they occur frequently These symptoms can usually be relieved by reassurance, rest and sedation (Phenobarbital, 06 to 03 gm four times daily), but occasionaly they are sufficiently severe and persistent to require active treatment A definite relationship has been found between anxiety states and episodes of premature beats, and it has been shown that they, as well as the distressing symptoms which occur during attacks, may, in some cases, be eliminated by adequate psychiatric therapy [214] Use of alcoholic beverages, excessive smoking or, in some individuals, even minimal smoking, may produce annoying episodes of "palpitations" as a result of premature ventricular contractions All smoking should be interdicted in these patients If drugs are necessary to stop premature beats, the physician should determine the site of origin of the ectopic beats before beginning therapy Quinidine is usually successful in reducing the frequency of both ventricular and atrial premature beats Pronestyl (procaine amide) is more effective in stopping or preventing ventricular premature beats than atrial premature beats. For example: a forty-two-year-old salesman began to experience frequent choking sensations associated with a momentary cessation of the heart beat and, on several occasions, he became faint an[illegible] most collapsed. Examina-

tion showed the heart to be normal but the electrocardiogram revealed ventricular premature beats. He received 250 mg of oral Pronestyl 4 times a day with prompt disappearance of the arrhythmia and has remained symptom-free since that time

Although this patient was controlled by 250 mg of Pronestyl four times daily, usually at least 500 mg is required orally every four to six hours to attain a similar effect.

Premature beats assume great clinical importance when they precede the onset of paroxysmal tachycardia, especially during operative procedures or following a coronary occlusion .

Chapter

2

ACUTE PULMONARY EDEMA AND CONGESTIVE HEART FAILURE

Many previously accepted concepts of cardiovascular and renal physiology and of sodium metabolism have been altered and new concepts of the pathologic physiology of heart failure and acute pulmonary edema have been introduced during the last ten years.

Pathogenesis of Cardiac Failure.—*In the past, the symptoms* and signs of congestive failure were attributed to "backward" failure, *i.e.*, myocardial insufficiency (cardiac failure), with increased venous pressure and venous congestion, increased blood volume secondary to anoxia of the bone marrow, and resulting edema.[300] Recent investigations, however, have shown that this mechanism does not explain many of the findings in congestive failure. These observations support the theory of so-called "forward" failure, *i.e., cardiac insufficiency, diminished cardiac output* and renal blood flow and decreased sodium excretion, with resulting increase in blood volume and edema.[222] Most of the symptoms and signs found in congestive failure can be accounted for by this sequence of events although they do not explain some of the findings in acute heart failure, *i.e.*, acute pulmonary edema (*vide infra*). When cardiac output falls, there may be a liberation of excessive amounts of antidiuretic hormone from the posterior pituitary gland[27] and of desoxycorticosterone from the adrenal cortex,[233] these

also play a part in the retention of sodium and water and contribute to edema formation. Although the pathogenesis of congestive heart failure has not yet been completely clarified, it is probable that elements of both the "forward" and "backward" hypotheses play a part in its development.

Excellent reviews dealing with the mechanisms of cardiac failure have been written.[64, 248, 267, 302] We wish, however, to emphasize certain facts presented in these papers concerning the patho-physiology of the various types of heart failure. A knowledge of these basic facts is essential for the intelligent handling of both the acute and chronic forms of this condition.

Heart failure occurs when the myocardium is no longer able to pump sufficient blood to all the tissues to satisfy their metabolic requirements. At first, the diseased myocardium is able to respond to stresses by increasing the length of its muscle fibers and contracting more forcefully (Starling's law of the heart).[300] Eventually, however, the fibers are distended beyond physiological limits and are no longer able to maintain an adequate output for tissue needs.

In congestive failure, the cardiac output may be low or normal as in hypertensive, arteriosclerotic or rheumatic heart disease, or it may be normal or high, as in thyrotoxicosis,[303] anemia,[303] beri beri,[51] Paget's disease,[78] arteriovenous fistulae[55] or chronic pulmonary disease.[268] In these latter conditions, although the output is not decreased, it still is unable to meet the tissue needs.[304] A primary object in therapy, therefore, is to increase the cardiac output. In cases of failure with low cardiac output this can often be done by decreasing the blood volume by means of salt restriction or phlebotomy. The resultant diminished venous return and lowered venous pressure enable the overdistended, inefficient cardiac muscle fibers to shorten to within physiological limits, to contract with greater force, and to increase stroke volume and output

In cases of failure with high output, correction of the primary condition usually brings relief.

Digitalis increases cardiac output in both types of heart failure although it is probably more effective in cases with low output[302] The drug acts directly on the heart muscle, increasing the force of its contraction,[56, 118] although the exact mechanism of the cellular change which improves myocardial contractility has not been determined. A primary effect on the venous system has been suggested[74] but this observation has not been confirmed.

Sodium retention is probably the most important factor in the production of the *symptoms* of congestive failure The retention of sodium and the consequent increase in total blood volume has been attributed to diminished cardiac output, diminished renal blood flow[231] and decreased renal excretion of sodium and water[224] A patient with heart disease may remain well compensated while his sodium intake is restricted but may quickly go into cardiac failure if given salt, the resultant increase in blood volume throws an additional load upon the already overburdened heart[218] Adequate salt restriction and the use of mercurial diuretics to aid sodium excretion are, therefore, of prime importance in the management of congestive failure

A marked increase in body activity increases the work of the heart and may cause a patient who was well compensated during rest or mild activity to go into severe cardiac failure It is important, therefore, to regulate a patient's activity carefully in order to avoid sudden episodes of cardiac failure The importance of *adequate rest*, either in a chair or in bed, especially during the initial period of treatment of heart failure, cannot be emphasized too strongly

If the above principles are borne in mind in the course of treatment of congestive failure, many lives will be saved and careless mistakes avoided, for example, phlebotomy is of great value in acute left heart failure secondary to hypertensive heart disease,[140] *i e*, cardiac failure with a low

output, but it may cause great harm if performed in other forms of heart failure, *e g*, heart failure associated with chronic anemia or arterio-venous fistulae In these latter conditions, a high output is necessary to maintain adequate tissue oxygenation, and measures that lower the blood volume, such as phlebotomy, should be avoided since they further decrease the amount of oxygen available to the tissues

Decreased renal blood flow, sodium retention and increased blood volume account almost entirely for the symptoms and signs of chronic congestive heart failure, *i e*, dyspnea, orthopnea, pulmonary congestion, distention of the neck veins, hepatomegaly, ascites, and peripheral edema Additional factors must be sought, however, to explain the sudden occurrence of acute left heart failure, *i e*, cardiac asthma and acute pulmonary edema

Paroxysmal Nocturnal Dyspnea.—Many patients with mild left ventricular failure experience recurrent episodes of paroxysmal dyspnea several hours after they retire They awaken suddenly and are acutely dyspneic, a few rales and pronounced wheezes appear over both chests, without other evidence of failure The blood pressure is high and the pulse is strong Breath sounds may be markedly diminished or absent over portions of the lung fields because of *intense reflex bronchospasm* *Paroxysmal nocturnal dyspnea*, commonly called cardiac asthma, is probably the result of a redistribution of blood with an increase in blood volume when the patient assumes the recumbent position During the day blood is pooled in the splanchnic and peripheral areas but when the patient lies down, blood is redistributed to the thorax[79] and lung congestion results As a result of this congestion, nerve reflexes from the lungs are initiated, and bronchospasm, dyspnea, and the other symptoms and signs of cardiac asthma result The exact mechanism of this condition has not been completely clarified

Complete relief is often obtained by having the patient sit up, stand, or walk about, if possible Mild cases may be controlled by aminophyllin suppositories (.5 gm., 7½ grains) This drug is safe when thus administered and is completely absorbed, and large doses may be given without producing significant discomfort The peripheral resistance is high in many of these cases because of sympathetic nerve discharge, and it may be necessary to give the aminophyllin intravenously (5 gm *slowly*).[158] In the more severe cases which do not respond to this drug, morphine sulfate should be given intramuscularly, 15 mg (¼ gr), or intravenously, 8 to 10 mg (1/8 to 1/6 gr) The intramuscular route is usually satisfactory. Morphine usually very effectively suppresses the pulmonary reflexes that serve to perpetuate symptoms If the attack persists, further treatment as outlined below for pulmonary edema should be carried out.

Recurrences of cardiac asthma can usually be prevented by the usual measures employed in congestive failure, *i e*, a low sodium diet, digitalization and mercurial diuretics, and by having the patient sleep on several pillows or in a chair, in the severe cases In some of the milder cases digitalization may not be required

Acute Pulmonary Edema.—The onset of acute pulmonary edema secondary to left ventricular failure may be extremely sudden with signs of circulatory collapse, severe dyspnea and cyanosis. It may occur following exercise, a large meal, paroxysmal tachycardia, a coronary occlusion, trauma to the central nervous system, or after severe emotional upsets.[147] A discharge of impulses from the sympathetic nervous system has been suggested as a possible explanation in the latter conditions [107] Occasionally pulmonary edema may complicate bulbar poliomyelitis. For this reason intravenous hydration should be carefully supervised in these cases.[327]

A good example of pulmonary edema induced by neurogenic factors is illustrated by a sixty-five-year-old woman who had experienced occasional attacks of pulmonary

edema three years before but had been quite well since then She recently witnessed her husband fall as a result of a cerebral hemorrhage and severely injure his scalp He quickly developed a left hemiplegia His wife did not appear anxious, but an hour later she suddenly began to wheeze and numerous rales appeared in both lungs She was given Demerol, 50 mg subcutaneously, and gradually improved

During the acute attack the heart sounds may be obscured by numerous bubbling rales and wheezes In many cases the right heart is strained by the failing left ventricle and the pulmonic second sound is accentuated When the patient is seen early, the blood pressure and pulse volume are often found to have been maintained A short time after the onset of symptoms, however, there is a marked fall in blood pressure and the pulse becomes rapid and thready, *i e*, shock occurs as a result of left ventricular failure Morphine sulfate should be given intramuscularly at once, or intravenously in cases with peripheral collapse in which little or no absorption would otherwise occur The doses employed are similar to those given in "cardiac asthma" This drug usually produces a dramatic improvement, but if no effect is noted, it should be repeated in fifteen to twenty minutes Dilaudid, 2 to 3 mg (1/32 to 1/20 grain), Pantopon, 20 to 30 mg (1/3 to 1/2 grain), or Demerol (100 to 150 mg.) may be used instead of morphine, especially if the latter induces vomiting Although some physicians use atropine, 0 4 to 0 6 mg (1/150 to 1/100 gr), routinely in the treatment of acute pulmonary edema, we do not believe that it is of value, in cases in which tachycardia is present it may actually be harmful

Despite the fact that the arterial blood is fully oxygenated in many cases, oxygen is of value in pulmonary edema.[10] Often, when given by the meter mask under pressure (3 to 6 cm), it produces dramatic results For example A thirty-year-old negress, para iii, with rheumatic heart dis-

ease, experienced mild toxemia of pregnancy. She was delivered of a full-term normal infant after a short labor but bled profusely and rapidly went into shock. She received 500 cc of plasma and 2500 cc. of blood within the next three hours after having lost an estimated 2000 cc of blood She recovered from shock but developed marked pulmonary edema one hour later. Despite repeated doses of morphine, oxygen by tent, 8 mg (4 cc.) Lanatoside C intravenously, and continuous bloodless phlebotomy with tourniquets, (*vide infra*), she did not improve. After one hour of vigorous therapy, oxygen under pressure (4 cm) was administered by the anesthesiologist and within ten to fifteen minutes marked improvement occurred The rales gradually disappeared and the patient recovered

To prevent recurrences oxygen may be given in this way for a period of fifteen minutes every few hours for ten to twelve hours after the episode of pulmonary edema has been controlled. An early recurrence is occasionally prevented by this therapy Oxygen by nasal catheter usually is not satisfactory, but an oxygen tent often is of value in warm weather It should be remembered that the percentage of oxygen inspired by a patient when a nasal catheter or tent is used is never so great as that inspired through a mask (35 to 65 per cent as compared with 50 to 100 per cent) There is some evidence that 100 per cent oxygen may be irritating to the lung parenchyma, particularly if taken for hours or days, for this reason the use of a lower concentration is advisable [153]

Intravenous aminophyllin, 0 5 gm. (7½ gr), is of particular value in the treatment of acute pulmonary edema when Cheyne-Stokes respiration is present When given by vein it should be administered very slowly, the total dosage being injected in forty-five to sixty seconds.

If the pulmonary edema persists in spite of the above measures 3 mg. of Strophanthin K or .5 mg. Ouabain (*Strophanthin G*) should be given intravenously. Cedilanid

(Lanatoside C) or Digoxin may also be used intravenously (the Digoxin preparation presently available may be used without diluting) Two cc of a mercurial diuretic should also be administered Thereafter, the Strophanthin is repeated if necessary or another digitalis preparation is used as outlined previously (Chapter I) When digitalis is given in elderly persons, the dosage employed should be less than in younger patients since sensitivity to the drug apparently is greatly increased in the aged Mercurial diuretics may be more toxic when used intravenously[166] but should be given by this route in acute emergencies, *e g*, when a patient is in shock and absorption is poor by other routes, the intramuscular or subcutaneous route should be employed thereafter

Bloodless phlebotomy by means of tourniquets,[178] if employed properly, may be effective in patients with pulmonary edema secondary to low output cardiac failure [197] Tourniquets are placed on three extremities and sufficient pressure is exerted to occlude the veins, but not the arteries Pressure is applied for fifteen to twenty minutes and then the tourniquets are released and rotated so that one extremity is always free of pressure The use of blood pressure cuffs instead of tourniquets presents some advantages in that the occluding pressure may be controlled Unfortunately, three or four cuffs may not be available in an emergency situation whereas some form of tourniquet always is obtainable If definite improvement does not occur after forty-five or sixty minutes, phlebotomy should be performed, 500 to 800 cc of blood being withdrawn rapidly Withdrawal of less than 500 cc rarely produces the desired decrease in blood volume, but if an adequate amount is withdrawn quickly, a resultant fall in venous pressure and a rise in cardiac output can be expected This increase in output occurs because the heart is once again able to respond to stress, *i e*, the decreased venous return allows the overdistended, ineffective

cardiac muscle fibers to decrease in size and contract more forcefully (within the limits of Starling's law of the heart). On the other hand, if the hemoglobin and hematocrit are definitely reduced, phlebotomy should not be considered. In fact, in pulmonary edema secondary to severe anemia with high output failure, small transfusions of packed red blood cells may be life-saving

The use of Hexamethonium, a ganglionic blocking agent (10 to 50 mg. intravenously), has been advocated for the treatment of acute congestive failure as a method of reducing venous return and relieving the overdistended myocardium without actually withdrawing blood[170] This drug produces vasodilatation and *peripheral* pooling of blood. There is no doubt that physiologically the use of hexamethonium is sound but its administration must be carefully controlled, and we do not believe that its routine use should be advocated for the treatment of a condition that can usually be controlled in other ways. It may be indicated, however, in patients with severe hypertension and failure

The use of antifoaming agents in the treatment of acute pulmonary edema has not been widespread despite enthusiastic reports of some observers[185] Alcohol vapor by inhalation penetrates the finer air spaces and alters the surface tension at the fluid-air interface, thereby collapsing the foam bubbles Success with this method of therapy has been noted after all other measures have failed Our own experience with this treatment has been limited, one of several patients so treated appeared to be helped

Acute Cardio-pulmonary Insufficiency.—The treatment of acute right heart failure associated with chronic pulmonary disease is extremely difficult and differs in many respects from the therapy of acute left ventricular failure[134]. Chronic emphysema and/or pulmonary fibrosis increase right heart work with resultant right heart hypertrophy (*cor pulmonale*). In the presence of overactivity, infection or emotional upset, acute right ventricular failure may occur.

Severe anoxia is usually present since the degree of oxygen exchange in the lungs is markedly curtailed The patient is cyanotic, he may be delerious or show other cerebral manifestations of anoxia and may be coughing up large amounts of thick sputum It is extremely important to maintain adequate respiratory exchange in these persons Morphine, codeine or the barbiturates are undesirable since they suppress respiration, but chloral hydrate or paraldehyde may be given if necessary If oxygen is administered in high concentrations, further suppression of respiration may occur and more CO_2 accumulate (respiratory acidosis) Oxygen may be given, however, provided that adequate respiration is maintained simultaneously by the use of respirators It may be necessary to treat the patent in this way for ten to fourteen days, utilizing the respirator ten to twenty hours a day Hospitalization and careful supervision are necessary Antibiotics should be given daily to combat infection, even if this is not clinically obvious The use of vaporized bronchodilators immediately and at frequent intervals may also be beneficial (Vaponephrin—5 to 10 drops in a nebulizer inhaled ten to fifteen minutes every four hours—has proved to be satisfactory) The patient should be digitalized, given mercurial diuretics and placed on a low sodium regimen in the same manner as in left ventricular failure Phlebotomy may be done in these patients in an effort to reduce blood volume since it is believed that the secondary polycythemic state is disadvantageous and is no longer a compensatory mechanism when the lesser circulation fails (The hematocrit should be kept at between 45 to 50 per cent and the hemoglobin at 12 0 to 12 5 gm) After recovery from an acute episode of cardio pulmonary insufficiency the patient should be placed on a careful regimen as outlined in a recent review on cor pulmonale [134] The treatment of this entity is far from satisfactory, but if the patient can be successfully treated during the acute phase, in many instances he may be carried for long periods

without difficulty. The prognosis in patients with cor pulmonale secondary to pulmonary fibrosis (silicosis, beryllosis, etc.), in which there is a fixed anatomical lesion, is less favorable than in those with emphysema in whom right heart failure is more easily reversible. Acute cor pulmonale may also be caused by pulmonary infarction or overwhelming pulmonary infection without chronic lung disease and these entities should be suspected in all cases with the above clinical picture.

Therapy of Congestive Heart Failure.—After the acute attack of failure is over, the usual management of congestive heart failure is instituted. Maintenance with a suitable digitalis preparation, *e.g.*, Digoxin, 25 to 50 mg, or gitalin, 50 to 75 mg per day (Chapter 1), *a low sodium diet and* the judicious use of mercurial diuretics are the three cardinal features of long term therapy. In addition, penicillin (300,000 to 600,000 u daily in a single dose) should be administered in cases of severe heart failure during the first few days when the degree of pulmonary congestion is considerable, in order to prevent secondary lung infections.[218] Dicumarol may be given to prevent the occurrence of phlebothrombosis and embolism, particularly in patients who will be bedridden for a long period of time.[137] The efficacy of this measure has been questioned by some observers, but in our experience the use of anticoagulant therapy has proved to be of value.

Adequate restriction of salt can now be achieved while the patient enjoys a reasonably well-balanced, palatable diet.[208] During the first week after the acute episode of heart failure, a diet containing less than 1 gram of sodium should be prescribed. This can be accomplished by allowing only fresh fruits, unsalted vegetables, potatoes or rice, cottage cheese, salt-free bread and salt-free milk, prepared from "lanolac" powder. Many patients do not tolerate "lanolac" milk but it may be made more palatable by the use of vanilla flavoring. This preparation provides a high

protein intake with minimal sodium in contrast to regular milk which has aproximately 500 mg of sodium in 1000 cc If the patient does well on this regimen, small portions of meat and fresh-water fish may be given The patient should be warned against eating the following foods:

Salt butter, margarine and peanut butter,
Crackers, cakes, pastries, or any food made with baking soda,
Smoked or salt cured meats and fish, ham, bacon, pork and corned beef,
Canned soups or vegetables,
Pretzels, salted nuts, potato chips, candy, beets, celery, lima beans, spinach and sauerkraut,
Olives, pickles, catsup, mustard and salad dressings.

A salt substitute containing potassium chloride may be used but most patients find this preparation bitter and unsatisfactory and prefer to use no salt at all. Palatability may be increased by flavoring with pepper, vinegar, garlic, onions, vanilla, chocolate, or cinnamon Many canned foods are now available as salt-free preparations This fact is plainly marked on the cans, and these foods may be included in the diet There should be no restriction placed upon the ingestion of water A fluid intake of 2 to 3 liters per day seems to be the optional intake for maximal sodium excretion [124,182] Tea, coffee, fruit juices, ginger ale, lemonade, salt-free milk (lanolac) and small quantities of alcoholic beverages may be taken. Frequent small meals are preferable to a few large ones, and under no circumstances should a large meal be eaten within two or three hours before bedtime. The patient should be cautioned against the use of sodium bicarbonate and hypnotics or laxatives containing sodium If a salt-poor diet, i e , a diet containing between 1 and 2 grams of sodium daily, is followed care-

fully, many recurrences of attacks of acute pulmonary edema or severe congestive failure can be eliminated *

It is very important for the patient to acquire the habit of *charting his weight daily*. Only in this way can the retention of small amounts of fluid be detected It is possible to accumulate from five to eight pounds of edema fluid before clinical signs (rales or ankle edema) appear

Patients who are obese should be put on a fairly rigid reducing diet We have seen patients with severe cardiac disease and intractable heart failure who were greatly improved and well controlled after marked weight reduction. Obese cardiac patients are much more difficult to control than those of average weight Great stress, therefore, should be placed upon weight reduction as an integral part of the therapy of congestive failure If these dietary precautions are observed, patients may be able to continue for many months without any additional therapy If, however, the patient is unable to adhere to a proper salt-poor diet, or if his weight increases or edema develops while on such a diet, *mercurial diuretics* should be used as often as is deemed necessary to keep the patient edema-free and at a stable weight

Intramuscular *Mercuhydrin* in 1 to 2 cc doses is a safe and effective mercurial which causes little pain at the site of injection It may also be used *subcutaneously Thiomerin*, a mercurial which is given subcutaneously, is also effective and easy to administer [17,127] It is possible to teach patients to administer it to themselves, as in the case of insulin administration

Another subcutaneous mercurial preparation that we have used and found to be a satisfactory diuretic is *Dicurin* (Merethoxylline).[54] Its potency is about equal to the other mercurial diuretics.

*An excellent low sodium diet booklet is available through The American Heart Association for a small fee

Since exercise increases sodium retention,[128] patients are instructed to stay in bed, if possible, for an hour or two following each mercurial injection during the early stages of therapy. In this way the maximum diuretic effect may be obtained. Occasionally minor muscle cramps occur two hours after the first dose of Thiomerin, but this discomfort disappears quickly. It is always best to administer diuretics parenterally during the initial period of treatment, and injections may be given daily for the first few days if the degree of failure is severe. Careful attention, however, must be paid to electrolyte balance in older persons.

Oral mercurial diuretics may be helpful in patients with congestive heart failure.[38] Their use had previously been limited because an effective preparation with few side effects (*e.g.*, gastro-intestinal disturbances) was not available. At present, however, several fairly satisfactory oral preparations are available and, undoubtedly, newer more improved agents will be developed in the future. In patients who require two or more injections of a diuretic weekly it is often possible to eliminate one of these by using an oral mercurial preparation. We have used Neohydrin (chlormerodin) frequently, and although approximately 30 per cent of patients developed signs of gastrointestinal irritation (cramps and diarrhea) and the drug had to be withdrawn, a significant number of the remaining patients were improved and required fewer injections of a mercurial. The usual dose of Neohydrin is two or three tablets daily. Recent studies have demonstrated that Neohydrin is a more effective diuretic than Cumertilin (mercumatilin), another orally effective mercurial. Usually the oral medication is not dependable enough to allow elimination of parenteral therapy, but occasionally a patient can be completely controlled by oral treatment. For example: A forty-three-year-old woman with rheumatic heart disease and mitral stenosis required the use of 2 cc. of mercuhydrin intramuscularly twice weekly despite a previous mitral

commissurotomy Adequate amounts of digitalis were being given (.5 mg. Digoxin daily) but she refused to remain on a satisfactory low sodium diet Neohydrin was administered in a dose of one tablet three times daily and parenteral therapy has been unnecessary for four months No side effects have occurred in this patient

Occasionally it is necessary to use ammonium chloride, 4 to 6 gms (60 to 90 gr) a day for two or three days, *prior* to mercurial administration to potentiate the mercurial effect. Enteric coated tablets, containing 1 gm each, given in small and frequent doses are fairly well tolerated, but the drug should not be used continuously or in patients with marked renal impairment because of the possibility of inducing severe electrolyte disturbances (hyperchloremic acidosis). Aminophylline, 0.5 (7½ gr) given intravenously increases renal blood flow and when used one to two hours after a mercurial diuretic may markedly increase the diuretic response [332] Mercurials may be given in the presence of renal disease unless oliguria or azotemia is present

Great care must be taken when administering mercurial diuretics to avoid excessive diuresis which may result in *salt depletion, dehydration* and *azotemia* [62 155] For this reason, it is wise to check the blood urea, sodium and chloride levels from time to time. When salt depletion occurs, it is often attended by serious chemical derangements and symptoms,[155,200] the most important of which are nausea, vomiting, cramps, extreme weakness, apathy, disorientation, stupor, coma and rarely, death A decreasing urinary output despite continued mercurial therapy is often a warning sign of impending difficulty. It is extremely important to recognize and treat the electrolyte disturbances which may occur as a result of the diuretic and low sodium therapy of congestive failure Early treatment of these reactions may be lifesaving. Several types of syndromes have been noted.[200]

(1) It has been repeatedly demonstrated that more chloride than sodium is excreted as a result of mercurial therapy. If diuresis is profuse, a chloride deficit may occur, producing *hypochloremic alkalosis* The blood sodium may not be decreased, the chlorides are usually below 85 mEq / liter and the CO_2 combining power is *elevated* In this situation immediate therapy is necessary Ammonium chloride, 4 to 8 gm., orally in divided doses or as a 1 per cent solution in glucose and water (100 cc /hour) or dilute hydrochloric acid (20 cc of U S.P 10 per cent acid in 600 to 1000 cc of water) may be given. (A glass tube should be used as a straw to avoid acid action on the teeth if hydrochloric acid is given) Ammonium chloride is given routinely by many physicians (3 to 6 gm /day) *during* the period of rapid diuresis to prevent the above complication It does not *potentiate* diuresis when used in this manner as it does when it is used *prior* to a mercurial injection

(2) If excessive quantities of both sodium *and* chloride are excreted during rapid diuresis, a *low sodium syndrome* is produced The blood sodium is usually below 125 mEq / liter and the chlorides are less than 85 mEq /liter The blood *potassium* is also decreased The use of hypertonic (5 per cent) sodium chloride intravenously with marked restriction of total fluid intake will usually correct this disturbance (86 mEq. of sodium in 100 cc 5 per cent sodium chloride) Potassium should also be given (2 to 6 gm /day as "Potassium Triplex," or solution of potassium chloride in citric acid or Karo syrup (see Chapter 1) by mouth, or intravenously (2 to 5 gm) given slowly in an infusion If a potassium deficit persists, arrhythmias secondary to digitalis toxicity may appear[195 291] since lowered potassium *increases* myocardial sensitivity to digitalis (Chapter 1).

(3) Other electrolyte disturbances are less frequently encountered (*a*) *hyperchloremic acidosis* (blood chlorides elevated, CO_2 combining power decreased), secondary to the excessive ingestion of ammonium chloride, is treated

by administering sodium bicarbonate or lactate. (*b*) Chronic *dilution hyponatremia* is accompanied by the presence of *intractable edema* without the symptoms noted in the "low salt syndrome." Therapy with hypertonic sodium chloride is unsuccessful and management in general is unsatisfactory.[318] The use of Southey Leach tubes or 14-gauge needles to eliminate the edema may be successful temporarily but the ultimate prognosis is poor

While the daily injection of a mercurial is usually effective in young persons, it may be dangerous for the elderly patient In older people only 1 cc of Mercuhydrin or Thiomerin should be given at most every other day *after* the acute attack of heart failure has been controlled In elderly men, mercurials often aggravate the symptoms of prostatic disease, causing acute retention and uremia [258] The use of an indwelling catheter in these cases will often alleviate this difficulty and diuretic therapy may be continued It has been demonstrated that morphine, Demerol,[98] quinidine, barbiturates, ephedrine, and Adrenalin often decrease the effectiveness of the mercurial diuretics and this fact should be kept in mind if any of these drugs must be given at the same time as a mercurial [98 114 217]

Occasionally during the course of active therapy with diuretic agents symptoms and signs of digitalis intoxication occur in patients whose digitalis dosage had been well regulated [170 254] This complication of mercurial administration is not stressed, but is probably much more common than previously suspected Although there may be some mobilization of digitalis with the edema fluid to account for this phenomenon, the urinary excretion of large amounts of potassium probably results in a sensitization of the myocardium to digitalis and in signs of digitalis toxicity. We have observed several patients whose digitalis dosage had been well regulated and who developed signs of digitalis toxicity, *i e*, nausea, vomiting, and ventricular premature

beats, within twelve to twenty-four hours after the initial dose of a mercurial diuretic.

The addition of Diamox,[181] a carbonic anhydrase inhibitor that increases the excretion of sodium, potassium and bicarbonate, to the number of oral diuretic agents presently available has helped in the management of *some cases* of cardiac failure. Our own experience, and that of others[182] *appears to indicate*, however, that unresponsiveness to the drug develops rapidly even with intervals of several days between doses. While the usefulness of Diamox as an *effective diuretic agent* appears to be limited, it is of value in the management of patients requiring constant diuretic therapy (1 to 2 tablets, 250 to 500 mg., three or four days each week).

The judicious use of the mercurial diuretics, adequate salt restriction and digitalization usually *control* cardiac failure. In some patients with refractory edema, however, or in others who are not able to stay on a salt-poor diet, the *use of cation exchange resins* may be justified, if given under close supervision. The resins are substances capable of "binding" ingested sodium within the intestinal tract and excreting it in the stools.[75] The ammonium cation exchange resins with added potassium are the most satisfactory and the danger of inducing acute *hypokalemia through the loss* of excessive potassium in the stools is minimized with this preparation.[170] Adequate renal function is a prerequisite to resin therapy if severe electrolyte disturbances are to be avoided. Although the use of exchange *resins alone does* not usually eliminate edema fluid, they may help to prevent its reaccumulation by removing most of the ingested sodium. If excessive amounts of sodium are allowed in the *diet, however, even large doses* of the resins will not successfully "bind" all of it. Cation exchange resins appear to potentiate the effect of the mercurial diuretics upon urinary sodium excretion.[83] Electrolyte disturbances are not frequent when the ammonium-potassium resin is used and

when careful attention is paid to blood electrolyte levels Constipation may prove to be an annoying symptom since large quantities of resin material must be ingested to produce an effect (30 to 45 gm. to eliminate approximately 1.5 to 2.0 gm. of sodium). Our experience with the exchange resins suggests that they may be a useful adjunct in the therapy of congestive heart failure only in selected cases

In addition to the above measures, the patient's activity should be carefully regulated Short periods of bed rest should be taken if symptoms become severe or if heart failure appears to be progressing

In heart failure secondary to hyperthyroidism, pernicious anemia, or nutritional deficiencies, the correction of the primary disease usually prevents its recurrence. In cardiac failure secondary to tachycardia treatment of the latter condition should be instituted, as outlined above Unusual etiologies of congestive failure should be eliminated before a case is labeled "refractory" to all therapy. An interesting example of this was a twenty-eight-year-old man who for eight years had been treated for increasingly severe heart failure Cardiac enlargement was present but no evidence of rheumatic, congenital, nutritional or metabolic heart involvement could be discovered A careful search led to the discovery of an arteriovenous aneurysm in the right buttock area (the result of a World War II shrapnel wound) Repair of the aneurysm led to a complete cure of his "refractory" heart failure.

In patients with heart failure, fluid may accumulate rapidly in the chest and cause acute distress In these cases immediate and repeated thoracenteses give remarkable relief and permit recovery Accumulation of fluid in the abdominal cavity also occurs but rarely does enough fluid collect to cause symptoms and require paracentesis This has been especially true in recent years since the use of palatable salt-poor diets and adequate mercurial therapy became widespread Occasionally, in patients with severe

rheumatic heart disease and long-standing congestive failure, massive ascites develops as a result of advanced cardiac cirrhosis, we have observed patients who required frequent paracenteses in order to remain comfortable One of these was a thirty-four-year-old female who was hospitalized because of chronic congestive heart failure secondary to rheumatic heart disease Bilateral pleural effusions and ascites were found Despite adequate digitalization, marked salt restriction and the frequent use of mercurial diuretics, little improvement was noted after one week of therapy. A paracentesis was performed and 7 liters of fluid were removed This was followed by a marked diuresis with dramatic clinical improvement Another paracentesis was done one week later, thereafter, the patient was controlled without "tapping"

Cardiac cirrhosis and liver disease in patients with chronic congestive failure are much more common than previously suspected,[30,105] and for this reason attention should be paid to the patient's intake of protein and vitamins Because these patients are often on a strict diet, there is a tendency to overlook simple measures such as the use of protein and vitamin supplements that might postpone the occurrence of severe liver disease and ascites

In extremely refractory cases of congestive heart failure the induction of hypothyroidism by the use of radioactive iodine is occasionally successful Another procedure that has been advocated for the treatment of refractory failure is ligation of the inferior vena cava[63,170] The operation has a definite morbidity and mortality, is merely palliative and the long term results are equivocal.

During attacks of acute heart failure, especially following coronary occlusion, hiccup, severe nausea, vomiting, and distention may develop and produce serious difficulties. It is of great importance to prevent these symptoms or, if they occur, to treat them quickly.

The excessive use of opiates should be avoided if possible, and laxatives should be given freely to avoid constipation

If frequent narcotics are being given, two and even three times the usual dose of a laxative may be necessary. If therapy with laxatives such as Milk of Magnesia (30 to 60 cc.) or Cascara sagrada (10 to 30 gr.) is not successful, occasional low gentle enemas should also be given. We have found the "Fleet's" enema preparation especially useful in these cases. Cathartics such as rhubarb that act upon the large bowel should not be used in patients receiving mercurials because of the possibility of inducing colitis.

The use of Dramamine and Thorazine*[111] (chlorpromazine hydrochloride, S.K.F.) have greatly facilitated the treatment of the nausea and vomiting that complicate congestive heart failure. Dramamine may be given orally, rectally or intramuscularly in a dose of 50 mg. Thorazine is given intramuscularly (10 to 25 mg.) for the first dose and then orally (10 to 25 mg. every six hours) until symptoms are no longer present. It is a most effective antiemetic agent. Transient postural hypotension and tachycardia may occasionally be noted after the first few doses. We have had great success with this drug. The sedative effect of Thorazine may also eliminate the necessity of using sedatives and narcotics while it is being given. (Thorazine potentiates the effect of these other agents if they *are* given simultaneously.)

Nausea and vomiting may occur as a result of overdigitalization or following the use of morphine, aminophylline or ammonium chloride. In these instances, the offending agent should be withdrawn.

The therapy of intractable hiccup is extremely difficult. Many drugs and maneuvers have been tried, each producing success at one time and failure at others. Sedation, amyl nitrite, intravenous niacin, inhalation of 5 to 7 per cent CO_2 and 90 per cent oxygen for a few minutes at a time, ethyl chloride spray to the region over the diaphragm,

*Chlorpromazine hydrochloride "Largactil" in Canada, England, France and Italy; "Megaphen" in Germany; "Ampliactil" in Argentina

inhalation of ether, or intramuscular quinidine, gr 6 (4 gm) three times a day[26] should all be tried in turn in the hope that one of them will be successful in stopping this debilitating symptom Thorazine in large doses (25 mg every four hours) may also be effective in some cases, perhaps largely due to its sedative effect A phrenicectomy or exeresis is occasionally required to stop a severe attack

Chapter

3

ANGINA PECTORIS, CORONARY INSUFFICIENCY AND CORONARY OCCLUSION

TREATMENT

THE most common cardiac emergency is pain in the chest First, it is essential to exclude extracardiac causes of chest pain such as spondylitis, gallbladder disease, peptic ulcer, hiatus hernia, esophageal spasm, herpes zoster, pneumothorax and pleurisy, before deciding that the pain is cardiac in origin This can usually be done by taking a careful history and doing a complete physical examination, but an electrocardiographic study may be necessary

Once the cardiac origin of the pain has been established, the type of acute cardiac episode must be determined The character, intensity and duration of the pain may help the physician to distinguish between attacks of *coronary insufficiency* (in which there is no acute closure) including *angina pectoris,* and *coronary thrombosis or occlusion.* In coronary occlusion the pain is usually prolonged, severe and unrelieved by nitrites, whereas, in coronary insufficiency, particularly angina pectoris, it is briefer and is relieved by nytroglycerin. Occasionally, however, coronary occlusion is associated with only mild pain and no other symptoms, whereas coronary insufficiency may cause severe pain. The entire clinical picture and the electrocardiographic changes should be considered before a definite diagnosis is made, and this frequently is possible only after observation for

several days. Any patient, therefore, who experiences sudden precordial pain, diagnosed to be cardiac in origin, should be put at rest and treated as a case of potential infarction, although many of these cases do not progress to a coronary occlusion with infarction

Angina Pectoris.—Angina pectoris is usually precipitated by effort, exposure to cold, excitement or large meals and represents temporary acute coronary insufficiency, with ischemia of the subendocardial layer but no myocardial necrosis. The ordinary episode of angina pectoris is quickly relieved by rest or nitroglycerin although the drug is not effective in over 10 per cent of cases A hypodermic tablet, gr 1/200 to 1/150, is taken under the tongue The patient should be instructed to take the nitroglycerin as soon as the pain appears If a specific activity, such as eating or walking in cold weather, is known to induce anginal pain, the drug should be taken prior to this activity For example, there are many patients who experience pain only in the morning on the way to the subway or train, a nitroglycerin tablet, placed under the tongue just before leaving the house often prevents the attacks This drug is safe and extremely effective, and should be taken as often as necessary There is no danger in giving nitroglycerin as frequently as every hour or even less The patient should be warned, however, not to take more than two tablets within five or ten minutes Additional tablets will probably not give relief and are apt to produce discomfort If the drug is not effective, one should suspect coronary occlusion

Occasionally a single nitroglycerin tablet produces flushing, intense throbbing and severe headaches, or even syncope, and, in these instances, a minute dose, gr 1/400 or less, should be used Even this dose may cause symptoms For example A forty-eight-year-old waiter suddenly experienced substernal pain and was given gr 1/150 of nitroglycerin Severe throbbing in the head, which lasted several hours, profuse perspiration and "faintness" occurred,

but the pain was not relieved During another attack of precordial pain, several days later, the patient was prevailed upon to try nitroglycerin again in a minute dose of gr. 1/400, but the same symptoms were produced

On rare occasions we have prescribed less than 1/400 gr to avoid a reaction While such a small dose may relieve pain, it is apt to be ineffective. Nevertheless, it is worth trying in a patient who can not tolerate a larger dose Also, a patient may react badly to nitroglycerin at one time but respond well at a later date

Some patients are averse to taking nitroglycerin because they have heard that it is dangerous or habit forming. It is essential to convince the patient that these notions are false and that the drug is not only effective but safe It is important psychologically that the patient take nitroglycerin, if it is not used, the pain tends to persist and the patient becomes frightened and anxious This state is apt to perpetuate the anginal syndrome by establishing a vicious cycle of pain, anxiety and more pain, often resulting in "status anginosus."

While nitroglycerin relieves anginal pain and can prevent it if it is taken immediately before a specific activity is undertaken, it is not effective in the general prevention of anginal attacks For this purpose we have found reassurance, frankness and optimism about coronary disease, some restriction of activity if necessary, loss of weight, eradication of irritating foci and sedation valuable Over the years many *vasodilator drugs*, particularly the xanthine group, have been used to prevent anginal pain without success

The latest drugs used, none of which has proven to be truly effective, include.

(a) PERITRATE (Pentaerythritol tetranitrate). A long-acting nitrate, has been found to prevent the appearance of coronary insufficiency following a 2-step exercise test,[272] but clinical studies have produced conflicting results and our experience has been disappointing.

At best, it appears to be effective only in an occasional patient in a dose of 10 mg four times a day

(b) METAMINE (Triethanolamine trinitrate biphosphate) Another long-acting nitrate, has proven of little value The dose is 2 mg four times daily [250]

(c) NITROGLYN A sustained action nitroglycerin tablet (gr 1/25 and gr 1/10) is said to allow release of the drug gradually over a period of ten to twelve hours As yet there are no published reports concerning this drug, but it has not been successful in our experience

(d) KHELLIN An extract from the seeds of an Egyptian plant, dilates the coronary arteries when given intramuscularly in a dose of 100 mg, or orally in 40 to 60 mg. doses three times a day Early favorable reports on this drug have not been confirmed[126, 247] and we have found that it usually produces nausea and vomiting in ordinary doses without relieving anginal pain

(e) PAPAVERIN DERIVATIVES Papaverin has been shown to be ineffective in the anginal syndrome in doses up to 800 mg daily [245] A derivative, *Pavertl Phosphate*, was recently introduced with an optimistic report but our own experience with this drug has been disappointing [228]

(f) HEPARIN Heparin has been given intramuscularly or intravenously two or three times a week, in doses of 50 to 100 mg, for anginal pain Although good results were reported initially, subsequent studies, adequately controlled, have shown the drug to be ineffective [228]

(g) QUINIDINE, TESTOSTERONE, VITAMINE E, (ALPHA TOCOPHEROL), HYDERGINE, NICOTINIC ACID, and AMINOPHYLLINE-ALUMINUM HYDROXIDE MIXTURES These have been used in angina pectoris, but without effect.

(h) RESERPINE (Rauwolfia serpentina) Occasionally effective in treating hypertension, has been used by us in

tense patients with angina pectoris without hypertension, and has appeared to help an occasional patient At times a patient experiences less pain with only one tablet a day

(i) ALCOHOL Although there is a prevalent notion that alcohol is beneficial in coronary disease and angina pectoris, there is no evidence that it produces dilatation of the coronary arteries[275] Occasionally alcohol relieves acute anginal pain when nitroglycerin is unavailable or ineffective. This effect is probably associated with the relaxation produced.

Status Anginosus and Angina Decubitus. During the course of a chronic anginal syndrome, there may be a sudden exacerbation of recurrent pain occurring at rest and at night, as well as on effort. This chain of events, known as "status anginosus," may follow an emotional upset and is usually a serious situation because the patient becomes very apprehensive as a result of the recurrent severe pain It is important to allay the patient's apprehension by reassurance, by using a strong sedative or a narcotic such as Dilaudid, gr 1/32 or 1/48 three or four times a day for seven to ten days, and by the liberal use of nitroglycerin for the pain Nitroglycerin usually relieves pain during this period of "status anginosus" which indicates that acute coronary insufficiency has occurred or that a coronary occlusion is forming or has formed If nitroglycerin becomes ineffective, coronary occlusion with major infarction has probably developed and the drug should be stopped immediately. During this period the patient should be at complete rest in a chair in his room.

While the period of "status anginosus" usually subsides after one to four weeks, occasionally the pain continues to recur frequently Also, occasional patients with a chronic anginal syndrome may fail to improve and continue to be unable to walk more than a short distance. In such refractory patients, three types of therapeutic procedures are

available to the physician. (*a*) lowering the metabolism with radioactive iodine (I_{131}), (*b*) interrupting the cardiac nervous pathways, (*c*) performing an operation to increase coronary flow and induce extracardiac collateral circulation

(*a*) RADIOACTIVE IODINE (I_{131})

This drug, which has largely replaced thyroidectomy[23] and antithyroid drugs,[267] is, of course, very efficacious in treating angina pectoris secondary to hyperthyroidism, but it may also be effective in relieving intractable angina in euthyroid patients.[30] In the latter, a hypothyroid state is induced but severe hypothyroidism may be prevented by careful regulation of the dose If severe hypothyroidism develops, it can be relieved by administering small doses of thyroid

According to some observers,[38] more than 50 per cent of patients thus treated are relieved of anginal pain The method is quite safe and may be tried in patients who do not respond to the usual methods of treating angina It must be remembered that the effect of I_{131} does not appear for at least one or two months after its administration If I_{131} is unavailable, propyl thiouracil may be employed using necessary precautions

A dramatic example of the effect of I_{131} in a euthyroid patient was a forty-six-year-old woman who developed an attack of acute coronary insufficiency with T-wave inversions She recovered completely and the electrocardiogram returned to normal She was free of pain for five years and then experienced frequent severe angina at rest and during the night She required 10 to 20 nitroglycerin tablets daily At this time her electrocardiogram showed T-wave inversion and on several occasions the inversion became deeper for seven to ten days Radioactive iodine tracer studies showed her to be euthyroid She received a therapeutic dose of I_{131} She continued to experience severe pain during the next seven weeks and since then has been free of

pain It is very likely that the improvement in this patient was the result of the I_{131} and was not spontaneous.

It is important to exclude the presence of actual hyperthyroidism in patients with severe angina pectoris, for only correction of the hypermetabolic state relieves the pain, as the following case report demonstrates.

A.F. was a sixty-seven-year-old Italian housewife who entered the hospital because of severe, recurrent episodes of substernal pain which began suddenly two weeks before Her blood pressure was 160/80, her rhythm was regular, and a grade ++ apical systolic murmur was heard The electrocardiogram showed deeply inverted T-waves in the standard and precordial leads, a diagnosis of coronary insufficiency was made In spite of complete bed rest and large doses of sedatives, she continued to experience frequent attacks of pain which were only partially relieved by nitroglycerin. During the course of a thorough study her basal metabolic rate was found to be +40 per cent, and she excreted only 10 per cent of a test dose of I_{131}, indicating hyperthyroidism She was given a therapeutic dose of I_{131} and after several days, Lugol's solution Her anginal seizures began to subside after several weeks and finally disappeared completely

(*b*) Interruption of Cardiac Nervous Pathways and Impulses

These procedures include, in the order of increasing seriousness (1) *paravertebral alcohol block* of the upper five thoracic sympathetic ganglia bilaterally, (2) excision of these ganglia (*thoracic sympathectomy*) and (3) laminectomy with section of the upper five dorsal roots (*posterior rhizotomy*).[310, 334] Sympathectomy appears to be the most effective of these and the operation is well tolerated.[90]

(*c*) Induction of Collateral Circulation to Increase Coronary Flow

A number of operative procedures devised years ago to induce collateral circulation between the heart and sur-

rounding tissues have been discarded,[68] however, the implantation of a substance such as talcum into the pericardial cavity (cardiopericardiopexy) is again in vogue in some quarters [313] An adhesive pericarditis is produced and although the degree of collateral circulation developed is a moot question,[46] symptomatic improvement has been reported in 50 per cent of patients [314] The operation is simple and the mortality rate is said to be low. Therefore, in the occasional patient with intractable angina who has not responded to radioiodine, the operation seems worthy of trial

Three other surgical procedures have been performed to increase coronary flow but must still be considered experimental and of unproven value They are

(1) Cardiac vein ligation to increase the blood flow through the Thebesian vessels [95]
(2) Arterialization of the coronary venous system by anastomosing the aorta to the coronary sinus by means of a venous graft [19]
(3) Arterialization of the intramural arteries by implantation of an internal mammary artery into the anterior wall of the left ventricle.[320]

It must be remembered that many patients with severe anginal pain, or even "status anginosus" which persists for many weeks or months, may eventually become symptom free on a good medical regimen Operation for angina pectoris should be considered only after all other therapy has failed and the effect of such a procedure has been carefully evaluated

Coronary Insufficiency.—Many acute coronary episodes are more prolonged than the transitory attack of angina of effort but less severe than a typical acute coronary occlusion. We have suggested that the name acute coronary insufficiency without thrombosis be restricted to these attacks [212,213] Although acute coronary insufficiency may resemble a mild coronary occlusion clinically they differ

electrocardiographically and pathologically In coronary insufficiency the electrocardiogram shows RS-T depressions and/or T-wave inversion in any leads (Fig 7), Q waves and RS-T elevation, which characterize coronary occlusion, are absent Acute coronary insufficiency may result in: (1) ischemia of the subendocardial layer, in which case the

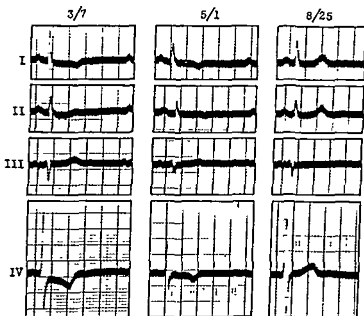


Fig 7—N G, m 53 Acute coronary insufficiency following physical exertion (Master and Jaffe, courtesy of Postgraduate Medicine)

electrocardiographic abnormalities disappear within several days, or (2) subendocardial necrosis, in which case the electrocardiographic changes may persist for weeks, and mild fever and elevation of the sedimentation rate may develop.

Acute coronary insufficiency represents a discrepancy between the supply and demand of coronary flow. It may

occur spontaneously or may be induced by conditions which increase the work of the heart, diminish the coronary flow or interfere with oxygenation of the blood These include effort, emotion, massive hemorrhage,[214] paroxysmal tachycardia, operative procedures or other conditions associated with shock or a drop in blood pressure (*e g*, intravenous pyelography or the use of anti-hypertensive drugs), acute infections such as gastro-enteritis, acute abdominal conditions such as cholecystitis and pancreatitis, hypertensive crises, pulmonary embolism and infarction, aortic stenosis and heart failure

Spontaneous Coronary Insufficiency.—The majority of spontaneous attacks of coronary insufficiency pursue a mild course and the prognosis is excellent In other cases, however, the attack represents the *premonitory phase of coronary occlusion* and the pain may recur for several days or weeks before the acute occlusion occurs [150] Careful observation is necessary with the patient at rest in a chair for one or two weeks If it is suspected that a coronary occlusion is forming, anticoagulants may be administered in order to prevent its completion but our results have been disappointing in this respect It is impossible to predict which cases will recover and which will go on to complete occlusion For example, Mr H began to experience repeated anginal pain at night and during the day His electrocardiogram showed mild T-wave changes He was given nitroglycerin and Dilaudid, his pain disappeared after several days and his electrocardiogram returned to normal This was a case of acute coronary insufficiency with spontaneous recovery

On the other hand, Mr S , who gave an identical history, was given Dicumarol but developed a coronary occlusion one week later.

The benign prognosis of spontaneous acute coronary insufficiency is illustrated by the following cases

Mr. I.F., a storekeeper, forty-four-years-old, had been observed over a number of years because of numerous functional complaints Physical examination, blood pressure, and electrocardiogram were normal. One day, while at work, he experienced severe substernal pain which lasted one hour and suggested the diagnosis of coronary occlusion He was not in shock, his heart sounds were regular and of good quality at a rate of 76. There were diphasic T-waves in leads I, II, and $V_{4,5,6}$ but his temperature was not elevated and there was no leucocytosis He remained asymptomatic but on the fourth day his sedimentation rate was elevated to 30 mm and his electrocardiogram showed· inverted T-waves in all leads, without Q-waves The T-waves gradually became upright and in four weeks the electrocardiogram was again normal He remained well during the next three years and his electrocardiogram was unchanged after exercise. *In this case the acute coronary insufficiency caused some subendocardial necrosis but recovery was complete*

A J, a sixty-three-year-old automobile salesman, with a history of bronchial asthma for many years, complained of sudden, severe pain across the upper back radiating anteriorly He perspired freely his blood pressure was 130/80, a drop of 30 points from his usual systolic pressure The pain lasted forty-five minutes and was then relieved by 100 mg of Demerol subcutaneously His electrocardiogram was normal and, after four days he was permitted in a chair He again began to experience frequent, severe pain in the upper back during the day and particularly at night Because an incipient coronary occlusion was suspected, Dicumarol therapy was begun and the patient received oxygen by mask, aminophyllin suppositories, Demerol 100 mg every four hours and sedatives The pain increased in severity but the patient's temperature, white count and sedimentation rate remained normal On the eleventh day the electrocardiogram showed slight inversion of the T-

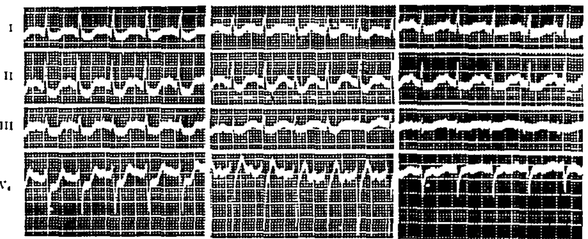


FIG. 8.—P.T., m. 58 Acute coronary *insufficiency in duodenal ulcer with profuse hemorrhage* Necropsy showed subendocardial necrosis A, Marked RS-T depression in all leads B, RS-T depression less marked C, Further improvement (Master, Dack, Horn, Freedman and Field, courtesy of Circulation)

waves in leads I and V_2 to V_5, but no other changes The T-wave inversion gradually increased during the following two weeks and then receded, four weeks after the acute episode the electrocardiogram had returned to normal. *The final diagnosis was therefore acute coronary insufficiency Although the temperature and sedimentation rate remained normal, subendocardial necrosis was doubtless present since the T-wave changes persisted for several weeks*

Coronary Insufficiency Secondary to Other Conditions.—One of the most frequent and important causes of acute coronary insufficiency is gastro-intestinal hemorrhage, particularly when there is a marked fall in blood pressure[214] (Fig 8). Prompt recognition and treatment are essential if the patient is to recover. Repeated transfusions may be necessary and we have not hesitated to give up to 2500 cc of blood in twenty-four hours, in order to keep the blood volume and blood pressure as close to normal levels as possible. As a rule these patients tolerate large amounts of blood well, should evidence of pulmonary congestion or edema appear, a mercurial diuretic is usually effective and digitalis should be given. The progress of the coronary insufficiency can be followed by serial electrocardiograms As improvement occurs, the T-wave inversions disappear. In the occasional fatal case, necrosis of the subendocardial layer is found but there is no evidence of acute thrombosis [106]

Every effort to prevent attacks of severe coronary insufficiency should be made in patients with evidence of coronary disease. They should be advised not to indulge in strenuous activities, they should also be warned against excessive eating, exposure to extreme changes in temperature, frequent sexual intercourse, emotional upsets and excessive smoking. It is important to prevent a fall in blood pressure, anoxia, tachycardia or hemorrhage when such patients are subjected to operation. If spinal anesthesia is used the blood pressure should be watched carefully and

neosynephrin given if the systolic pressure falls below 100 mm Hg If considerable bleeding occurs, blood for a transfusion should be readily available

In diabetic patients with coronary disease who are receiving insulin it is important to prevent episodes of hypoglycemia, it is better to allow them to spill small amounts of sugar than to attempt to attain perfect sugar control, since hypoglycemic reactions may precipitate episodes of coronary insufficiency. If the above precautions are followed many cases of this syndrome will be prevented

Coronary Thrombosis or Occlusion.—In coronary thrombosis a fresh thrombus obstructs the lumen of one of the major coronary arteries The pain experienced in coronary occlusion usually begins suddenly, at rest, during sleep or in the course of routine activity It is usually precordial or substernal, but may be situated only in the back of the chest or neck, or in the arms Instead of pain, the patient may complain of severe burning sensations or feelings of tightness, nausea, vomiting, and profuse perspiration Varying degrees of shock may be present The sudden onset of paroxysmal tachycardia or pulmonary edema is occasionally the first evidence of an acute coronary occlusion Examination may reveal gallop rhythm, embryocardia, (tic-tac rhythm), or congestion of the lungs. The blood pressure may be normal at first or it may drop precipitously

The clinical and electrocardiographic manifestations of coronary occlusion depend upon the pathological changes that occur in the coronary arteries and myocardium In over half the cases the process of thrombosis is initiated by a subintimal hemorrhage which leads to secondary changes in the intima or completely occludes the vessel lumen [147] This process of thrombus formation may take days or weeks. During this period the patient may experience severe episodes of angina or recurrent pain at rest, the so-called "premonitory phase" of an occlusion.[156] The electrocardiogram may show RS-T depressions and T-wave inversions, indi-

cating coronary insufficiency with myocardial ischemia. These changes are replaced by Q waves and ST segment elevations, however, as soon as the occlusion has become complete (Fig 9) In coronary occlusion a Q-wave usually

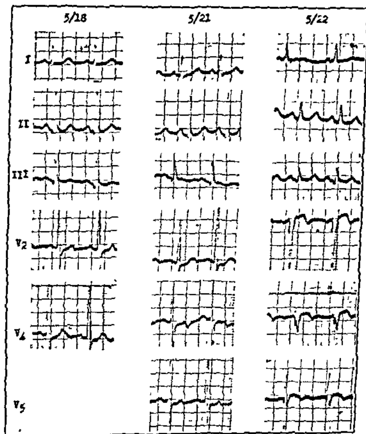


FIG 9—N H, m 45 RS-T depression and T-wave inversion in the chest leads, indicating coronary insufficiency, during the premonitory phase of coronary occlusion (5/18, 21) Following the acute attack RS-T elevation and Q-waves appeared in leads V_2 and V_4 (5/22), indicating anterior infarction (Jaffe, courtesy of J Mt. Sinai Hosp)

appears in one or more leads, depending upon the site of the infarction, and produces a characteristic pattern of a Q-wave and RS-T elevation (Fig 10). During the following days and weeks, serial tracings reveal a progressive return of the RS-T segment to normal, and an inversion of the T-wave, resulting in a Q, inverted T pattern which may persist for months or years Fever appears on the second or third day, the sedimentation rate becomes prolonged by the fourth day, often to 50 mm or more Since the infarction is "through and through," the subpericardial region is

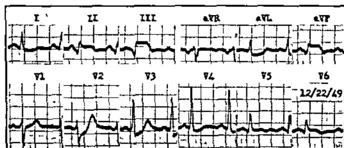


FIG 10—J S, m 58 Acute coronary occlusion with postero-lateral infarction (Master and Jaffe, courtesy of Postgraduate Medicine)

involved, and a pericardial reaction[308] and friction rub may result The infarct also reaches the endocardium, therefore mural thrombi may form and peripheral emboli develop [138] In coronary insufficiency without thrombosis the necrosis is limited to the subendocardial area and only RS-T depression and/or T-wave changes occur

At times it is difficult to distinguish between a coronary occlusion and acute pericarditis Some of the features that differentiate these conditions from one another and from coronary insufficiency are summarized in Table 5 The most reliable distinguishing feature is the presence of Q waves in the electrocardiogram, which are characteristic of

coronary occlusion. It is important not to mistake pericarditis for coronary occlusion since anticoagulant therapy is contraindicated in acute pericarditis, for the reason that hemorrhagic effusion may occur.

In treating *coronary occlusion,* it is essential to relieve the pain as soon as possible If it is not very severe, Demerol,

Table 5. Differential Diagnosis of Acute Coronary

	Pain	Severe Shock	Gallop Rhythm	Pericardial Rub	Heart Failure	Arrhythmias	Drop in Blood Pressure
A Coronary Insufficiency a) Mild—Angina Pectoris	Few seconds to 10–15 minutes	Absent	Usually absent	Absent	Absent	Absent	Absent
b) More Severe—Spontaneous or Secondary	May be prolonged	May be precipitating factor, e.g. hemorrhage	May occur	Absent	Uncommon except in cases due to tachycardia	Uncommon	Moderate if episode precipitated by hemorrhage or tachycardia
B Coronary Occlusion	Usually severe longer than 15 minutes, rarely absent	Present in about 10 per cent of cases	Common	Not uncommon Usually transitory Often localized	Common	All types common	Often marked
C Pericarditis	Mild, occasionally severe Often related to respiration	Rare	Rare	Usually present Often widespread Often persistent	Uncommon	Atrial flutter and fibrillation not uncommon	Rare unless cardiac tamponade occurs

50 to 100 mg subcutaneously, usually suffices. For more severe pain, morphine, 15 mg (gr. 1/4) subcutaneously or 10 to 15 mg. (gr. 1/6 to 1/4) intravenously, may be required. The intravenous route is the more effective. The drug may be repeated in the same doses in twenty to thirty minutes The possibility of inducing distention, obstipation, nausea and vomiting with morphine is great and the dose used should not be larger than is actually required.

Morphine should be discontinued if any of the above symptoms appear since distention and vomiting may turn an otherwise benign course into a stormy one If the patient is receiving oxygen there is little danger of respiratory depression. We have used Dilaudid extensively and have found it to be a reliable analgesic which produces fewer

Insufficiency, Coronary Occlusion and Pericarditis

Fever	Leukocytosis	Elevated Sedimentation Rate	ECG RS-T El RS-T Dep Q Waves	Pathology	Precipitating Factor	Treatment
Absent	Absent	Rare	RS-T El Absent RS-T Dep Transitory Q-Waves Absent	No pathological changes	Emotion, exercise, cold large meals, etc	Nitroglycerin In status anginosus-narcotics for short period
May be present	May be present 10,000–15,000	Mild to Moderate	(RS-T El Rare) RS-T Dep Common Q-Waves Absent	Subendocardial *necrosis* often present	1) Tachycardia, *hemorrhage*, shock, trauma and as in angina pectoris 2) Spontaneous	1) Treat etio*logical* factor 2) Symptomatic
Usually present after 24 hours May be high	Usually present after 24 hours, may be over 15 000	Usually after 72 hours Often very high	RS-T El Common (RS-T Dep Reciprocal) Q-Waves Common	Through and through infarction of myocardium	None (except shock*)	Symptomatic anticoagulants (see text)
Common at onset	Depends on etiology If viral leucopenia	Common at onset	RS-T El Common (RS-T Dep Rare) Q-Waves Absent	No myocardial damage (may be subepicardial)	Nonspecific (viral?) rheumatic fever bacterial traumatic tuberculous, other diseases	Treat primary disease

unpleasant and dangerous side effects than morphine Two and one-half to 5 mg (1/24 to 1/12 gr) usually relieves pain We have also found Pantopon and Metapon satisfactory. Nitroglycerin does not relieve the pain of acute coronary occlusion and should not be used since it may further lower blood pressure and decrease coronary blood flow

Oxygen should be given by tent or mask when the pain

persists after morphine has been given A tent usually induces less apprehension than does a mask. Occasionally, intravenous aminophylline 5 gm, (7 5 gr) is of value It should be injected slowly. In rare instances, sodium amytal, .5 gm (7 5 gr.) by vein has been effective when all other measures have failed

As soon as the pain has been controlled, the question of *hospital* or home care arises The vast majority of patients can be cared for at home, unless conditions there are unsatisfactory. Visitors other than the immediate family and the use of the telephone should be banned Patients with a coronary thrombosis are apprehensive and discouraged It is extremely important to encourage them, stating frankly that they have had a coronary attack but that most patients make a complete or satisfactory recovery and lead full lives [219]

The most serious complication of coronary occlusion is *shock* which in the past was almost always fatal

The mechanism of "*cardiogenic shock*" is not entirely clear but it has been shown that in acute myocardial infarction there is a reduction in cardiac output[214] and stroke volume and severe, generalized vasoconstriction.[102] This may produce not only a state of shock but also fluid retention and heart failure. Theoretically the use of transfusions and intravenous fluids is not indicated and, in fact, has proven of little value although they only rarely induce heart failure [88 276] Intra-arterial transfusions have also been found to be ineffective [29]

The outlook in "cardiogenic shock" in the past few years has considerably improved as the result of the use of vasopressor drugs When these are administered *within the first few hours,* occasional patients have recovered The drugs used include: (1) Norepinephrin (Levophed) [277] This must be given slowly by the intravenous route (4 mg. in 1000 cc. glucose in water) The infusion should run rapidly enough to maintain the systolic pressure at approximately 100 to

110 mm Hg, avoiding higher levels The drug is continued as long as the pressure tends to fall without it Levophed is safe if its effect is carefully observed Its major effect is on the blood pressure although it may increase cardiac irritability to some extent and rarely cause arrhythmias Localized superficial gangrene, as a result of intense vasoconstriction, has been observed in several patients who had received Levophed for long periods The drug often exerts a rapid and marked effect, as the following case demonstrates Mr D developed a coronary occlusion and diaphragmatic infarction and his blood pressure did not rise above 90/70 mm for five days A Levophed intravenous infusion was then started with 4 mg per liter, forty-five minutes later his blood pressure was 170/120 The rate of flow was then slowed as much as possible in order to keep the systolic blood pressure below 120 (2) Mephentermine (Wyamine) The dose is 10 to 20 mg intravenously, or 15 to 35 mg. intramuscularly repeated as often as indicated (every thirty to forty-five minutes) Wyamine does not affect myocardial irritability[45] (3) Phenylephrine (Neo-synephrin)[99] 1 mg intravenously or 5 to 10 mg intramuscularly, repeated every hour or two, if necessary, and (4) Methoxamine (Vasoxyl),[244] 20 mg intravenously or intramuscularly, have also been used with success

The use of these drugs requires constant observation but the time spent will be amply repaid if even a small percentage of patients recover from this very serious condition One of these drugs should be in the doctor's bag, for the sooner the treatment is instituted the better the outlook

A patient in shock should immediately be placed in a moderate Trendelenburg position and oxygen administered if available The patient is usually apprehensive and, particularly if pain is present, a narcotic should be administered In those cases with pulmonary congestion or other evidence of *congestive failure*, intravenous Strophanthin or Cedilanid should be administered as previously described[99] (Chapter

1) In some instances clinical signs of heart failure may be absent, yet the venous pressure, if determined, is found to be elevated Consequently, if a patient in shock does not respond to vasopressor drugs and the other measures described above, it is worthwhile to administer digitalis for occasionally the result is gratifying.

Clinical evidence of mild *left ventricular failure* is very commonly observed early in the course of coronary occlusion, a few rales are found in the chest and slight congestion of the lung fields is seen on x-ray. As a rule, this type of failure requires no specific therapy but responds promptly to moderate salt restriction and to an injection of a mercurial diuretic Not infrequently, however, acute pulmonary edema is the first or only sign of a coronary occlusion, or severe heart failure develops within several days after the acute episode As an example of the former, we observed a woman of sixty-four who suddenly developed attacks of severe pulmonary edema but who had experienced no chest pain whatsoever Nevertheless, the electrocardiogram revealed evidence of an acute coronary occlusion with myocardial infarction. Doubtless, this had occurred at the time of the first attack of pulmonary edema.

If pulmonary edema occurs, the treatment is as outlined previously for *pulmonary edema* in the absence of coronary occlusion (Chapter 2), *i e.*, morphine or another narcotic and, if necessary, intravenous aminophylline, intravenous Strophanthin or Cedilanid, oxygen, a mercurial diuretic, and phlebotomy unless a severe state of shock exists.

The treatment of *congestive failure* in coronary occlusion is the same as in chronic heart disease although there is some difference of opinion concerning the use of digitalis Many physicians believe that it should be used in coronary occlusion whenever heart failure is found,[105] but some, including one of the present authors, prefer to use diuretics and a low salt diet before administering digitalis and, if necessary, to digitalize somewhat more slowly than usually.

This does not hold for an acute emergency like pulmonary edema. Caution in the use of digitalis in coronary occlusion is exercised because of the potential danger of inducing *arrhythmias*, particularly ventricular tachycardia

Arrhythmias of all types occur frequently in coronary occlusion. The most common are *premature beats* and *paroxysmal atrial fibrillation, flutter* and *tachycardia* They do not appear to alter the prognosis very significantly since they often are of brief duration and remit spontaneously For this reason it is not necessary to begin specific treatment of these arrhythmias immediately if the patient is comfortable Sedatives should be used liberally because the tachycardia is apt to cause anxiety If the arrhythmia does not cease within one-half to one hour, specific therapy should be instituted as outlined in Chapter 1 If there is any indication of incipient heart failure or shock at the onset of the arrhythmia, treatment should be started promptly.

The temporary nature and spontaneous remission of paroxysmal tachycardia in coronary occlusion is illustrated in the case of M W , a retired businessman of seventy-nine, who developed a coronary occlusion with anterior infarction and did well for two days On the third day his heart rate suddenly increased to 160 The electrocardiogram showed a supraventricular tachycardia with bundle branch block The arrhythmia was remittent at first but then became constant and the patient developed dyspnea It was decided, therefore, to administer intravenous Cedilanid, 4 mg , but, by the time this had been drawn into the syringe, the arrhythmia had ceased and did not recur If the drug had been administered, relief of the arrhythmia would have erroneously been attributed to it

Ventricular tachycardia is a more serious and persistent complication in acute coronary occlusion It usually responds to Pronestyl or quinidine and these drugs should be given promptly as outlined above (Chapter 1). A par-

ticularly difficult case treated successfully with Pronestyl was M.G., a sixty-year-old tailor with a history of duodenal ulcer who was admitted to the hospital because of melena and hematemesis of several days' duration. For several months he had experienced pain in his left arm on effort and this symptom increased following the onset of bleeding Physical examination was negative but the electrocardiogram showed an acute coronary occlusion with anterior wall infarction and regular sinus rhythm His course was uneventful until the twelfth day when he suddenly became dyspneic and perspired profusely His heart rate was 190 and the rhythm was slightly irregular The electrocardiogram showed a ventricular tachycardia The patient received morphine, intravenous quinidine, .65 gm, (10 gr.) on two occasions, intravenous magnesium sulfate and intramuscular quinidine without effect. He developed congestive failure within twenty-four hours and was given Mercuhydrin and Digoxin, 1 5 mg by mouth, with some improvement He then received quinidine, 4 gm (6 gr) every two hours by mouth The rate of the ventricular tachycardia ranged between 130 and 140. On the third day of the arrhythmia he was given 1 gm (15 gr) of procaine amide (Pronestyl) intravenously in fifteen minutes. During the injection a few sinus beats appeared but the tachycardia recurred a short time after the drug had been discontinued The next day, 2.25 gm of Pronestyl were injected intravenously in thirty-five minutes and numerous sinus beats appeared. Within two hours regular sinus rhythm appeared and the patient made an uneventful recovery.

Many years ago it was suggested[188] that quinidine be routinely administered early in coronary occlusion to prevent ventricular tachycardia We do not subscribe to this view because, in our experience with 1000 cases of coronary occlusion who did not receive digitalis, ventricular tachycardia occurred in only .5 per cent.[210] We, as well as

others, do not believe that it is necessary routinely to employ a drug such as quinidine with potential toxic effects in an attempt to prevent a complication which is infrequent.[96] We do, however, administer quinidine or Pronestyl if numerous premature beats appear, particularly if they are multifocal.

Varying degrees of partial or complete A–V block are not uncommon following coronary occlusion.[211] *P–R prolongation* is usually not significant and remits spontaneously. *Partial heart block* with dropped beats and *complete A–V block* occur with diaphragmatic infarction and are more serious. If Stokes-Adams seizures occur, treatment should be carried out as outlined in Chapter 1.

Although Adrenalin is ordinarily avoided in coronary occlusion, it is effective and should be used if Stokes-Adams attacks intervene, as the following case demonstrates. A forty-nine-year-old man was admitted to the hospital because of recurrent attacks of unconsciousness and substernal pain for two weeks. On examination, he appeared critically ill. His ventricular rate was 28 and the auricular sounds were audible at a rate of 100. His blood pressure was 170/70, as it was being taken, the patient developed convulsive movements and the cardiac sounds became inaudible. He recovered from the attack in a few seconds. An electrocardiogram revealed complete A–V block (Fig. 11). He was given Adrenalin (1:1000), .4 cc. every two hours. On the third day he developed congestive failure and the electrocardiogram showed flutter fibrillation. He received 6 mg. Digitoxin and 2 cc. Mercuhydrin intravenously and the Adrenalin was discontinued. The next day he developed another Stokes-Adams seizure, the Adrenalin was resumed every 2 hours. Nevertheless, the attacks recurred several days later and the Adrenalin was given every half hour or hour. He improved and the frequency of the Adrenalin injections was gradually diminished. It was again increased one week later when the attacks recurred, and Adrenalin

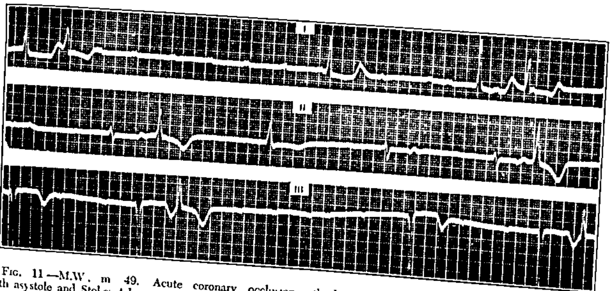


Fig. 11.—M.W., m 49. Acute coronary occlusion with diaphragmatic infarction Complete A-V block with asystole and Stokes-Adams seizures Treatment consisted of epinephrine mg 5 to 10 q ½ h for several days

could not be discontinued until two months after admission Thereafter, the Stokes-Adams attacks did not recur although the complete A–V block persisted

Anticoagulant Therapy.—Considerable difference of opinion exists today concerning the use of anticoagulant drugs in acute coronary occlusion. After their introduction less than 10 years ago, several reports indicated a significant decrease in embolic phenomena and mortality rate[341] and their use became routine in coronary occlusion unless a specific contraindication existed The rationale for their use was partly based on post-mortem reports which placed the incidence of pulmonary and peripheral emboli in coronary occlusion between 45 and 60 per cent.[112,118] In the past few years, however, as the result of the clinical observation of increasing numbers of mild cases, it has been suggested that anticoagulant drugs are unnecessary in such attacks[274,285] In our experience, the mortality rate in first attacks of coronary occlusion in private patients is less than five per cent Other observers have found the mortality rate in all mild attacks to be 3.1 per cent and believe that the use of anticoagulant drugs is unjustified in such cases since the incidence of embolic phenomena is very small and accounts for no more than 1 per cent of fatalities.[274]

Our experience is now in accord with this point of view. In recent years we have not used anticoagulant drugs in mild cases of coronary occlusion and have obtained excellent results

Anticoagulant drugs are indicated. (1) when congestive failure or shock is present, (2) if there is a history or evidence of peripheral phlebitis, (3) following pulmonary embolism or infarction, (4) following peripheral embolism, (5) in obese or debilitated patients whose movements are restricted or who may require prolonged bed rest. Pulmonary emboli usually originate in the lower extremities and lodge in the lower lobes.[205] It is possible that a small percentage arise in the

Table 6.—Differential Diagnosis of Pulmonary Embolism and Coronary Occlusion.

	Pain	Dyspnea	Severe Shock	Hemoptysis	Heart Sounds	Pericardial Rub	Fever	ECG	X-Ray
Pulmonary Embolism	often absent, not typical	often severe	common in cases with large infarcts	Not uncommon	P_2 often accentuated	absent	may be high	a) RS-T depression T-wave inversion (Coronary Insufficiency) b) S_1, Q_3 pattern c) Right BBB	Hazy patch in lower lobe may be present
Coronary Occlusion	usually severe, substernal, precordial, left arm	often mild or absent	occurs in 5–10% of cases	absent unless pulmonary edema present	gallop rhythm common	may be present in about 10% of cases	usually not over 101°–102°	RS-T elevation & Q waves Serial changes	may show minimal congestion

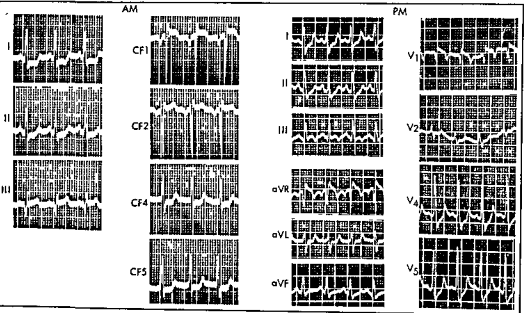


FIG 12—E V, F 40 Acute pulmonary embolism fifteen days following pelvic operation Death nine hours later Necropsy revealed bilateral pulmonary embolism of right main and left lower lobe branches The posterior papillary muscle of the left ventricle showed focal necrosis *AM*—Record taken soon after onset showed RS-T depressions *PM*—Record several hours later showed prominent S-wave in leads I and II and RS-T rounding in lead III (Dick Master Horn Grishman and Field, courtesy of Am J Med)

right auricle in the presence of atrial fibrillation or prolonged congestive failure The symptoms of pulmonary embolism are very variable There may be severe chest pain, dyspnea and collapse simulating coronary occlusion, or merely cough, fever or tachycardia (Table 6) Electrocardiographic abnormalities are present in half the cases, the most common single pattern being that of coronary insufficiency, *i e*, RS–T depression and T–wave inversion[67] (Fig 12) Other patterns consist of a deep S_1 and Q_3 with RT_3 elevation, and occasionally right bundle branch block Pulmonary emboli usually do not occur until after the first week of the attack, most commonly during the second week About one-third of the patients with pulmonary embolism expire within a few minutes or hours despite all treatment, if a patient survives more than three or four hours he probably will recover.[318] In some cases it is difficult to distinguish between pulmonary embolization and fresh myocardial infarction The following points are helpful in making a differential diagnosis. (1) Although fever, tachycardia and chest pain may be present in both conditions, and cough may occasionally occur in cases with coronary occlusion and mild congestive heart failure, the presence of cough and hemoptysis favors the diagnosis of pulmonary embolism (2) Calf tenderness or a positive Homan's sign[146] indicates the presence of a thrombotic process in a lower extremity and, therefore, possible pulmonary embolization (3) A loud pulmonic second sound, not previously heard, may indicate pulmonary hypertension secondary to infarction, and the finding of a hazy patch of infiltration on chest x-ray may further suggest the diagnosis of an embolic episode (4) The electrocardiographic changes described above may be present in pulmonary infarction and simulate a posterior wall infarction but a Q–wave is absent in aVF All of these findings may help to distinguish between the two conditions Occasionally, pulmonary infarction occurs during the course of a coronary

occlusion without the appearance of chest pain, cough and electrocardiographic findings In these instances, a persistent, high fever or leucocytosis may suggest the diagnosis

If one of the indications for anticoagulant therapy is present, heparin should be given by injection for an immediate effect[259] and oral therapy with Dicumarol,[12] Tromexan[47 136 260] or Hedulin[34] begun for a later effect As soon as the oral medication has prolonged the prothrombin time to therapeutic levels, (in 24 to 48 hours), the heparin is discontinued

Heparin may be given subcutaneously, 100 mg every eight hours, intramuscularly as Depo heparin, in an initial dose of 400 mg, or intravenously, 50 mg every four hours around the clock. In the above dosage heparin usually prolongs the clotting time to approximately double the control value, i e., from fifteen to twenty-five minutes (Lee White method) and there is ordinarily no danger of hemorrhage. The clotting time should be determined immediately before, and two hours after, the first dose of heparin, in order to discover patients who are sensitive to it Thereafter, this determination is unnecessary If Tromexan or Hedulin is used, it is usually unnecessary to administer more than one or two doses of subcutaneous or intramuscular heparin If hemorrhage does occur in the course of heparinization, a 1 to 2 per cent solution of protamine sulfate is given by vein in a dose of 1 mg of protamine per mg of heparin

The administration of oral anticoagulants requires much closer supervision than does heparin, since there is a tremendous variation in the response to them from person to person and, in the same person, from day to day Even after some stabilization of dosage appears to have been achieved, further administration of the drug in some cases produces unpredictable effects Therefore, during the first two weeks of treatment the prothrombin time should be determined daily, before the next dose is given If Dicumarol is used, an initial dose of 300 mg followed by 150 to 200 mg. the

next day is usually quite safe, but we have observed several cases in which one dose of 300 mg of the drug prolonged the prothrombin time to dangerous levels For example L.W., a woman of twenty-eight with chronic rheumatic valvular disease, mitral stenosis, congestive failure and atrial fibrillation, experienced several episodes of peripheral embolization. Following a recent one, she received 300 mg of Dicumarol on the first day and 200 mg on the second Her prothrombin time was thirty-six seconds on the third day, and no Dicumarol was given on that day or the next On the fourth day diffuse ecchymoses appeared over the entire body, and her prothrombin time was ninety-four seconds *She received 2 doses of 72 mg of intravenous* vitamin K within five hours and the prothrombin time fell to normal limits within eight hours An uneventful recovery followed.

M R, a garage owner of fifty-six, developed a coronary occlusion He received 300 mg of Dicumarol on the first day and 200 mg on the second His prothrombin time rose to fifty-two seconds and did not fall during the following two weeks, although he received no more of the drug

These cases illustrate the extreme variability of response that may occur following Dicumarol therapy

In Dicumarol therapy, the prothrombin time should be maintained at 2 to 2½ times the control time, *i e.*, between twenty-five and thirty-five seconds. In most patients this result is achieved with a daily dose of 50 to 150 mg The urine should be inspected grossly every day and urinalyses should be done every two to three days, if a significant number of red cells are found in the urine, the dosage should be reduced or the drug temporarily stopped. If the prothrombin time is prolonged to sixty seconds or more, or if bleeding occurs, the drug should be stopped and the patient given intravenous vitamin K_1 oxide,[229] in a dose of 50 mg. *The emulsion of vitamin K_1 oxide may also be given orally Usually the prothrombin time will return toward*

normal levels within four to eight hours. If K_1 oxide is unavailable, intravenous vitamin K (72 mg) should be given every four hours until the prothrombin time is shortened to safe levels. In severe cases, frequent transfusions of fresh blood are invaluable

Because of the danger of hemorrhage, anticoagulants should not be administered to patients with a history of hepatic, gastric or renal disease, to those with a hemorrhagic tendency, or in the presence of ulcerative colitis or a cerebrovascular accident

Occasionally a patient develops hemorrhage while on anticoagulant therapy despite the fact that his prothrombin time has been reported to be within safe limits A good example of this was the case of a fifty-eight-year-old man who developed a coronary occlusion with anterior wall infarction and was given 300 mg and 200 mg of Dicumarol on the first two days On the fourth day his prothrombin time was twenty seconds but he passed a large tarry stool, and his hemoglobin fell to 8 6 gm He was given a small transfusion slowly and recovered quickly

Hemorrhage may occur into serous cavities, even into the pericardium.[121,154] It is important to remember that anticoagulants are contraindicated in nonspecific pericarditis since they may cause pericardial hemorrhage It has even been suggested that they be withheld in coronary occlusion, when a definite pericardial friction rub is present, since pericardial hemorrhage with cardiac tamponade has been observed in one or two such cases following anticoagulant therapy It is occasionally difficult to differentiate nonspecific pericarditis from coronary occlusion during the first few days of the attack (Table 5); if there is any doubt, anticoagulants should not be administered

Anticoagulant therapy should be maintained through the period of bed rest and for 5 to 7 days afterward. Some physicians continue it indefinitely for months or years in order to prevent a recurrence of coronary thrombosis.[217] *The value of this procedure has not been proven.*

In no instance should oral anticoagulant therapy be instituted unless facilities are available for reliable prothrombin time determinations. Even if these are present, occasional mistakes are made in determining the prothrombin time and, therefore the clinical picture should be closely observed

Other Oral Anticoagulants.—Of numerous oral preparations recently introduced, only two have proven useful clinically. Tromexan,[47, 136, 280] an ethyl ether of Dicumarol, acts much more quickly than the latter drug and is not cumulative Its effect is apparent in eighteen to twenty-four hours and maximum in thirty hours. Therefore, when it is used with heparin, the latter may be discontinued after the first day The dose of Tromexan is five or six times that of Dicumarol, *i e*, the initial dose is 1500 to 1800 mg and the maintenance dose 300 to 900 mg Although its rapid action is desirable, Tromexan has proved to be less satisfactory than Dicumarol, because of the greater variability in individual reaction and in daily maintenance dose and the sudden, unpredictable changes in prothrombin time.[419, 326] In general, therapy with Tromexan requires more careful control than with Dicumarol *Hedulin* (Phenylindandione)[32] also acts more rapidly than does Dicumarol, exerting its maximum effect in twenty-four to thirty-six hours Its action is dissipated in twenty-four to forty-eight hours. The initial dose is 300 mg for patients over 150 lbs. and 200 mg. for those weighing less [32] The usual maintenance dose is 50 to 100 mg. The daily dose is divided in two, given in the morning and at bedtime Final evaluation of the drug is not yet possible because there have been no reports of its use in large, well controlled series of patients with coronary occlusion.

If peripheral arterial embolization occurs, despite anticoagulant therapy, the anticoagulants are continued In cerebral embolization, however, great caution must be observed in administering these drugs, if a spinal tap does not reveal hemorrhagic fluid, anticoagulant therapy may be

carried on after several days. Sedation should be avoided in these patients and caffeine sodium benzoate, 7½ gr. (.5 gm.), intramuscularly every four hours, and aminophyllin 3 gr. (.2 gm.), intramuscularly every four hours, may be given. Other supportive measures should be employed: oxygen should be used, and parenteral feedings continued until the patient is able to feed himself.

When a peripheral embolism occurs, intra-arterial Priscolme, 50 to 75 mg., every four to six hours, given proximal to the occlusion, is sometimes of value in increasing circulation in the affected extremity.[200] Various ganglionic blocking agents also produce a high degree of vasodilatation and reduce vasoconstrictor tone when administered subcutaneously or intravenously. We have found that Hexamethonium (Bistrium-bistrimethyl-ammonium hexane dibromide), produces a longer lasting blockade than other presently available drugs.[246] Hexamethonium (25 mg./cc.) may be administered in doses up to 1 to 2½ cc. subcutaneously or intravenously every four to six hours to maintain an adequate blockade. The drug should be given cautiously in patients with hypertension. It is best to begin with small doses in order to avoid a precipitate drop in blood pressure. The patient should remain recumbent one and one-half to two hours following each injection. In our experience this type of therapy has largely replaced nerve blocks in these patients since the performance of the latter in patients on anticoagulant therapy may induce hemorrhage. If the patient is able to tolerate oral therapy, the measures outlined above may be supplemented by the use of Priscoline, 50 to 75 mg., or Dibenzyline, 10 to 20 mg., every four hours.[120, 230] If the patient is seen after gangrene has occurred, the leg should be packed in ice, in preparation for amputation.

Embolectomy is the treatment of choice if it can be performed within eight to twelve hours after the acute episode. In expert hands results have been good, and even

massive saddle emboli lodged at the bifurcation of the aorta have been removed successfully[168] It is a serious operative procedure, particularly in patients with recent myocardial infarction, but it is justified unless the patient is critically ill A patient recently observed illustrates the fact that embolectomy can be performed successfully, even in the presence of serious heart disease

A sixty-three-year-old tailor developed an acute coronary occlusion with anterior infarction He did not receive Dicumarol On the fifth day he complained of severe pain in the right leg which became mottled and cold up to the mid thigh The femoral pulse was not palpable Five hours after the onset of symptoms operation was performed by Dr. Gabriel Seley, of New York and an embolus was removed from the femoral artery Complete function of the extremity was restored, and the patient made an uneventful recovery

If embolectomy is not feasible and amputation becomes necessary, it should be performed under local or block anesthesia, after demarcation has occurred

Length of Bed Rest —There has been considerable difference of opinion as to how long patients with acute coronary occlusion should be kept at strict bed rest. For many years a period of six weeks in bed was considered essential in all cases in order to allow a "firm" scar to form[203] and at present many physicians insist upon four weeks lest a ventricular aneurysm develop[283]

Recent observers however, have emphasized the fact that prolonged bed rest is often unnecessary in acute coronary occlusion or heart failure, and, in fact may have harmful effects.[76,183 184 185 239] It has been shown that recumbency tends to increase cardiac work by raising the circulating blood volume.[256] In addition to producing serious psychological tensions, prolonged bed rest causes generalized loss of muscular and vascular tone, constipation and distention, and predisposes to venous thrombosis[73]

For these reasons many physicians now allow patients running a mild course to use a commode early in the attack and to sit in a chair after one or two weeks Others however, have advocated the armchair treatment from the first day or two, particularly when *heart failure* is present but *not* when severe, prolonged shock or cerebral or peripheral embolism exists [184,185] Follow-up reports indicate that patients so treated do not develop ventricular aneurysms more frequently than do others [230] It should be emphasized that the armchair regimen does not involve early ambulation, the patient is helped or lifted into a chair and is returned to bed in the same way after a number of hours This treatment of acute coronary occlusion will have to be evaluated over a longer period with well controlled studies before a final opinion may be reached

At the present time each patient should be treated *individually* It is evident that the mild case may be treated liberally and may be expected to make a good recovery. If such a patient objects to the bedpan, he may be permitted to use a bedside commode and, once he is up, to sit in a chair On the other hand, if a patient running a mild course does not mind a short stay in bed, we are inclined to keep him in bed one week and then to permit him to sit in a chair While in bed, he is advised to move his legs and may feed himself

A more important decision must be made, in respect to the armchair treatment, in patients who are more seriously ill with congestive failure, tachycardia, persistent hypotension of 80 or less or a state of mild shock Such patients should be treated in bed with the usual therapeutic measures If failure is present, every effort is made to approximate the sitting position by using a hospital type of bed or by placing 9 inch blocks under the headposts. If the patient fails to improve, the effect of placing him in a chair may be determined

Ambulation —If the course of a coronary occlusion has been mild and the patient has been sitting in a chair during the first week, we usually permit him to walk by the third week. Such a patient is usually ready to return to work in two or three months In the more severe cases a patient may not be ready to walk for four to six weeks or to resume working for three to six months Four out of five patients who have recovered from a coronary occlusion lead productive lives for many years.[219]

We do not depend upon the electrocardiogram or sedimentation rate to determine the severity of the attack or when the patient may sit up, walk about or go back to work If the patient is asymptomatic and the clinical findings are satisfactory, ambulation is permitted although the electrocardiogram shows marked alterations In some cases, we do not wait for the electrocardiogram to become stable While a very abnormal sedimentation rate is of diagnostic value early in the attack, we have observed serious cases with little elevation, as well as cases with a high sedimentation rate for months or even years during which time they have been active and well

A normal ballistocardiogram following coronary occlusion usually indicates a good recovery but the patient may be doing very well when his ballistocardiogram is definitely abnormal.[237] It must be remembered that the ballistocardiogram may be abnormal in people over 50 without heart disease

Nausea, Vomiting, Distension and Hiccough —These are common disturbing and serious symptoms in acute coronary occlusion The suggestions for prevention and treatment outlined in Chapter 2 should be followed

Chapter

4

SYNCOPE

SYNCOPE or fainting is a common symptom and occurs in many non-cardiac conditions (Table 7) Only occasionally is it caused by organic heart disease or cerebral arteriosclerosis Syncope is the result of temporary cerebral anoxia which is most frequently produced by a marked decrease in peripheral resistance and fall in blood pressure, the cardiac output being fairly well maintained This type of syncope or fainting is termed neurogenic or vasodepressor [102] Fainting occurs because in the upright position pooling of blood occurs primarily in the lower extremities A less frequent mechanism of cerebral anoxia and syncope is a sudden drop in cardiac output, as occurs following severe hemorrhage [42] Not infrequently both mechanisms, *i e.*, a drop in blood pressure and in cardiac output, are present Other specific causes of syncope include postural hypotension, hysteria and anxiety states, hypoglycemia and severe coughing bouts[271] or bearing down efforts

It is usually possible to determine the type of syncope if the characteristics of each are borne in mind (Table 7)

(*a*) *Neurogenic or Vasodepressor Syncope*—This is the commonest type of syncope. It is associated with reflex peripheral vasodilatation which may be precipitated by the sight of *blood*, *fright*, pain or a severe emotional disturbance [66] Not uncommonly it is induced in the doctor's office by the sight of a hypodermic *needle* for an injection or at the Red Cross or a hospital when the needle is to be inserted

Table 7.—Differential Diagnosis and Treatment of Syncope

Type	Precipitating Factor	Premonitory Symptoms	Duration of Attack Convulsions?	Findings	Treatment
1) Vasodepressor Syncope a) Neurogenic	Fright, pain, emotional upset sight of blood	Nausea, sweating, light-headedness, dizziness, (only occurs when patient is standing), premonitory phase 1–5 minutes	Usually of short duration, 1–15 seconds—after 15 seconds twitching may appear	Cardiac output normal Blood pressure falls Pulse rate may rise or fall Electroencephalogram abnormal	Usually terminated by laying patient down with head lower than feet Rarely .5 to 1 cc Epinephrin (subcutaneously) if necessary
b) Carotid Sinus Syncope	a) Pressure on neck b) Turning head c) Cerebral arteriosclerosis d) Digitalis	*Usually no* premonitory symptoms	Short duration Convulsions may occur	Blood pressure falls Pulse rate decreases Electroencephalogram abnormal	Ephedrine Sulfate 25 mg t.i.d Probanthine 15 mg or Atropine 3 mg t.i.d Excision of sinus nerves if attacks are severe and persist
c) Secondary to Other Factors	Internal or external hemorrhage, *e.g.* in peptic ulcer	Same as (a)	Same as (a)	Cardiac output diminished	Treat primary condition
2) Postural Hypotension	a) Tabes dorsalis b) Spinal cord tumors c) Addison's disease d) Diabetes mellitus e) Standing in one place, arising suddenly f) Idiopathic	Light-headedness, dizziness	Usually of short duration (1–5 seconds) No convulsions	Blood pressure falls Pulse rate increases Electroencephalogram abnormal	Lay the patient down Elastic stockings, tight abdominal belt and neosynephrine or ephedrine Tilt bed, high Na diet, DOCA Caution against rising quickly Treat primary disease
3) Hysterical Syncope	a) Suggestion b) Pressure on any area of body, c) Tense situation d) Hyperventilation	*No premonitory symptoms*	*Never any convulsions* *May last for hours*	No change in blood pressure or pulse rate No electroencephalogram changes	Psychiatric
4) Cardiac Syncope	a) Aortic stenosis b) Heart block with periods of asystole c) Ventricular tachycardia	Dizziness, palpitation chest pain nausea, epigastric pain	Usually short (5–10 seconds) May last longer with convulsions	Electrocardiographic abnormalities Blood pressure falls Pulse rate may be extremely slow rapid or imperceptible	For cardiac arrhythmia, Quinidine, Digitalis Pronestyl For heart block, Epinephrin, Isuprel, Atropine Pacemaker
5) Hypoglycemic Syncope	a) Islet cell tumor b) Overactive pancreas c) Too great an interval between meals d) Hepatic disease	Weakness extreme hunger tiredness, sweating, pallor	May be prolonged if not treated Convulsions occur frequently	Blood sugar extremely low Electroencephalogram abnormalities Pulse rate increased Blood pressure unchanged or low	Intravenous glucose, then oral glucose—depending upon etiology (see text) a) remove tumor if present b) low carbohydrate diet c) high cabohydrate diet if liver disease is present
6) Tussive Syncope	a) Severe coughing b) "Bearing down"	Dizziness tightness	Short (1–5 seconds)	No unusual findings	Warn patient against "bearing down," or excessive coughing while standing

in the arm during blood donation Syncope resulting from peripheral vasodilatation may also be observed in people who, while sitting or recumbent, employ *heating pads* for low back pain, or who have been sitting or reclining in the hot sun When they suddenly assume the erect position, temporary cerebral anoxia occurs and fainting may result Syncope also occasionally occurs in normal persons who are required to stand in one place for long periods of time

Vasodepressor syncope is more frequent in men than in women Premonitory symptoms such as nausea, sweating, or lightheadedness usually precede the attack, which occurs only if the patient is standing This type of syncope can usually be terminated by having the patient lie down with his head lowered This is far more effective than placing the head between the knees If the syncope lasts more than ten to fifteen seconds, clonic twitching may appear, but true grand mal seizures are extremely rare In this type of attack it is sometimes necessary to administer vasoconstricting drugs, e g, epinephrine, 5 cc of a 1 1000 solution, subcutaneously, or neosynephrin, 5 to 10 mg, intramuscularly

An important type of vasodepressor syncope to bear in mind is encountered in persons with a *hypersensitive carotid sinus* It is not uncommon for such people to faint when the sinus is massaged[274] but only a small percentage do so spontaneously Consequently, a diagnosis of *carotid sinus syncope* should be made only if the following criteria are satisfied (1) The attacks must occur without the premonitory signs usually seen in other forms of vasodepressor syncope, e g, those associated with fright or the sight of blood (2) The attacks should be reproducible by sinus stimulation (3) The attacks should not occur after the administration of adequate doses of atropine or ephedrine, i e, doses large enough to prevent bradycardia on manual carotid sinus stimulation True cases of carotid sinus syncope are relatively uncommon when compared with other types of vasodepressor syncope

An interesting illustration of carotid sinus sensitivity was furnished by a seventy-one-year-old man who was admitted to the hospital because of four attacks of syncope during the preceding four months. Examination revealed a blowing

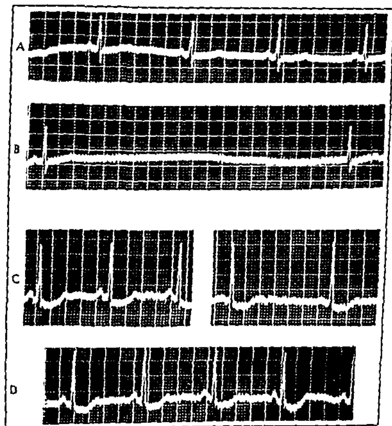


Fig 13—J Q, m 61 Arteriosclerotic heart disease Continuous lead II A, Control, sinus bradycardia, rate 52. B, After pressure on left carotid sinus Asystole for four seconds followed by nodal beat C, Following oral atropinization and compression of right carotid sinus D, Compression of right carotid sinus following intravenous atropinization

systolic murmur at the aortic area, transmitted into the neck The blood pressure was 160/80 The peripheral pulses were not palpable. The electrocardiogram showed evidence of a previous lateral wall infarction In the hospital he experienced brief episodes of dizziness At first it was thought that his syncope was the result of cerebral arteriosclerosis and aortic stenosis Pressure on the right carotid sinus, however, produced asystole and a drop in blood pressure to 80/60 The patient became blanched, his hands twitched and he yawned Stimulation of the left carotid sinus produced similar results, but with less regularity. He was given oral atropine, 3 mg. (gr 1/100) q i d. and, after several days, carotid sinus pressure failed to cause a change in his heart rate (Fig 13) The patient has been maintained satisfactorily on this medication. It was difficult to establish a diagnosis of true carotid sinus syncope in this case, despite the fact that definite hypersensitivity of the sinus could be demonstrated, since the patient had cerebral arteriosclerosis and aortic stenosis, which alone may have caused the syncope Since atropine definitely prevented the attacks, however, the diagnosis of syncope secondary to carotid sinus sensitivity was the most logical one

Patients who have extensive arteriosclerosis or are receiving digitalis are more susceptible to syncopal attacks and, in some instances, stopping digitalis eliminates the attacks completely Carotid sinus syncope may be induced by pressure on the sinus from any cause, *e g*, by an enlarged gland in the neck, by a sudden movement of the head while shaving, and by sitting with one's head leaning *on his hand*

Tight collars may serve as a trigger mechanism. J C, a thirty-eight-year-old midwestern preacher, was investigated because he had fainted several times while delivering his Sunday sermon In eliciting his history it was discovered that during the week he worked in the field with his collar open,

on Sunday, however, he wore a stiff collar to appear in church. Carotid sinus pressure repeatedly induced asystole and syncope in this patient, and the attacks were eliminated when the patient stopped wearing tight collars.

Convulsions may occur as a result of excessive carotid sinus stimulation[141] and caution must be observed when testing a patient for sensitivity, particularly an older person with arteriosclerosis. Pressure should be applied unilaterally for not more than ten seconds and the patient should be recumbent when tested. Ephedrine sulphate (25 mg.), Paredrine (60 mg.) or atropine sulphate three times a day prevents most attacks. Atropine is given in tablets of gr. 1/50 to 1/100 or 10–15 gtt. Tr. Belladonna until dryness occurs. Recently Banthine (50 mg.) or Pro-banthine (15 mg.) three times a day has been advocated. Neosynephrine, in oral doses of 10 to 20 mg. three times a day, is occasionally successful when other medications fail. When it is necessary to use sympathomimetic drugs, *i.e.*, ephedrine, for long periods of time, it is wise to administer small doses of a sedative (barbiturates) simultaneously to prevent nervousness and insomnia. In a few cases, excision of the sinus has given permanent relief.[153]

(*b*) Postural hypotension is associated with poor sympathetic nervous regulation of blood vessels.[40,305] It may occur in normal persons, in patients with neurocirculatory asthenia and in those with serious underlying central nervous system disease,[84] such as cord tumor or tabes dorsalis.[298] It is common following sympathectomy and the use of autonomic blocking drugs for the treatment of hypertension. We have also observed extremely severe postural hypotension in patients with advanced diabetes mellitus, Addison's disease and pheochromocytoma. When these people assume the upright position, blood is pooled in the lower extremities and, as a result, the normal compensatory splanchnic constriction does not occur, the cardiac output is diminished and the blood pressure falls. Hyperventilation

has recently been suggested as a factor in postural hypotension syncope [48]

In patients with chronic postural hypotension and recurrent syncopal episodes, therapy is extremely difficult A primary disease should be sought and treated if possible, *i e*, Addison's disease If no underlying condition is found, the most effective method of prophylaxis is the application of elastic bandages around the legs and thighs. A tight abdominal belt may also be helpful Atropine, epinephrine, neosynephrin or Paredrine may be tried, in the doses cited, but have not proven very successful They are usually more effective when used in conjunction with leg or abdominal binders At times it may be temporarily helpful for these patients to sleep in a bed tilted 20 to 25 degrees from the horizontal with the head up,[201] in order to train the vasomotor system to vasoconstrictor activity Desoxycorticosterone acetate and sufficient salt to cause slight dependent edema sometimes reduce the frequency of attacks. The patients should be instructed to rise from bed slowly and to avoid taking drugs that cause peripheral vasodilation, *i e*, amyl nitrite or nitroglycerin

A severe instance of postural hypotension was recently observed in a forty-two-year-old woman She also exhibited anhydrosis and miosis which suggested a central type of sympathetic nervous system defect, presumably in the hypothalamus An identical clinical picture has been noted by us in patients receiving chemical sympathetic blocking agents, *e g*, Dibenzyline A response to sympathomimetic drugs was not obtained, however, in this patient, and it was necessary to maintain her on six to eight grams of added salt and 5 to 10 mg of Desoxycorticosterone daily She has done remarkably well on this regimen although ankle edema has appeared intermittently

(*c*) Fainting may be *hysterical* in origin, particularly in women This type of syncope is not accompanied by premonitory symptoms and is not associated with any

changes in pulse or blood pressure. These patients may fall to the ground and remain unconscious for a period of several seconds or hours, but convulsions do not occur and injury rarely results. Electroencephalographic changes, which are seen in most other forms of syncope that last more than a few seconds, do not appear in this condition [56] Fainting may be precipitated by suggestion or by manipulation of almost any part of the body Therapy is mainly psychiatric

In anxiety states syncope occasionally occurs as a result of *hyperventilation* Such an attack may be reproduced by having the patient breathe deeply for one or two minutes Assurance and sedation are the only treatment of value in correcting this condition

(*d*) A rare form of syncope is that which follows severe bouts of *coughing* or the Valsalva maneuver (a forced expiration with the glottis closed—the "bearing down" effort) [2,30] A marked rise in intrathoracic pressure occurs and prevents adequate filling of the right atrium, resulting in a marked fall in cardiac output and cerebral anoxia Recognition of this type of syncope is important since most of these attacks can be prevented by warning the patient against excessive bearing down efforts, such as straining at stool, and against remaining upright during a spell of severe coughing

(*e*) Fainting which occurs early in the morning before breakfast or several hours after a meal may be the result of *hypoglycemia* This type of syncope is seen in cases of hyperinsulinism caused by pancreatic adenomata, in patients on a high carbohydrate diet with an overactive pancreas, and in cases of advanced hepatic disease [58] The patient usually experiences weakness, dizziness and extreme hunger before fainting, convulsions often occur if therapy is not instituted quickly Intravenous or oral glucose should be given as soon as possible and recovery from the attack is usually rapid. The diagnosis is made from the history, the fasting blood sugar determination and the glucose tol-

erance test Extremely low blood sugar levels may be obtained during the course of the latter test, particularly in the two-, three-, and four-hour specimens, and fainting may occur before the test can be completed. These attacks may be prevented in several ways, depending upon the etiology of the condition (1) If hypoglycemic attacks occur before breakfast, and rarely during the day, and if liver damage is demonstrated, a high carbohydrate, high protein diet should be prescribed (2) If the attacks occur before breakfast and frequently during the day, and if they become progressively more severe and are not relieved when the patient is put on a low carbohydrate, high protein diet, a pancreatic adenoma is probably present and surgical removal of the tumor is advisable (3) If the attacks occur approximately two to three hours after meals, and if no evidence of liver disease or progression is found, so-called "functional" hypoglycemia is present, and the patient should be put on a low carbohydrate, high protein diet with frequent feedings Additional points of differentiation between these three major types of hypoglycemia and suggestions for therapy may be found in a recent review [58]

(*f*) In *organic heart disease*, syncope may occur in complete A–V block or calcific aortic stenosis (Chapter 1) and, rarely, it may usher in an acute coronary occlusion It is not uncommon at the onset of any type of paroxysmal tachycardia, whether functional or associated with heart disease [57] For example, a man of forty-nine was recently hospitalized for recurrent syncope of unknown etiology. After several days he fainted and, when he was seen, almost immediately, atrial fibrillation was present It ceased in a few minutes The prognosis of syncope naturally is more serious in heart disease than in non-cardiac conditions.

Cardiac syncope is most frequent in *calcific aortic stenosis*, whether rheumatic, congenital or sclerotic, and usually follows exertion It should always be kept in mind as a possible cause of syncope A pertinent case was a woman

who began to experience occasional syncope in her eighties. A harsh aortic systolic murmur was present but her hemoglobin was less than 10 gm., and it was thought that the anemia was the cause of her syncope However, although the anemia responded to therapy, she continued to experience syncopal attacks and the aortic murmur increased in intensity After several years she developed recurring Stokes-Adams seizures and died within several days, doubtless as a result of the aortic stenosis

In the past, aortic stenosis resisted all treatment once it had advanced beyond a certain stage Recently, however aortic valvulotomy has been performed in several hundred patients[9] Although satisfactory results have been reported by some authors, the mortality rate of this procedure is quite high and it requires further evaluation.

(g) *Cerebrovascular Disease* Vertigo and syncope are not infrequent in the course of chronic cerebrovascular disease, and at times may indicate the occurrence of a small hemorrhage or thrombosis Such patients should be observed and treated symptomatically

Chapter

5

RHEUMATIC FEVER AND HEART DISEASE

During the acute stage of rheumatic fever the occurrence of acute pericarditis, congestive failure and, occasionally, arrhythmias necessitates emergency treatment In such cases early adequate treatment often reduces the morbidity and mortality rate Previously, only salicylates and symptomatic treatment were available in rheumatic fever With the advent of *ACTH* and *Cortisone*, it seemed at first that a dramatically effective form of therapy had been found[346] At present, however, medical opinion is fairly well distributed among those who claim that these drugs are very effective, those who claim that they have little or no advantage over salicylates and those who believe that they may be effective but that this has not been proven as yet[207] It is generally agreed that these hormonal drugs suppress the inflammatory reaction in rheumatic fever Fever and arthritis usually subside in one to three days and the sedimentation rate returns to normal in 10 to 20 days Tachycardia and gallop rhythm are less consistently affected Some authors have claimed that the adrenal cortical hormones also suppress severe carditis if administered early, but the majority have not found this to be true Murmurs have been observed to develop in patients treated with these drugs[344] Although the question is not yet settled, it appears that ACTH and Cortisone do not prevent the development of chronic valvular disease following rheumatic fever

While their action in rheumatic fever remains a moot question, ACTH and Cortisone should be used when the salicylates appear to be exerting little effect or when the symptoms are severe They should be continued for at least two to three weeks The initial daily dose of ACTH is 100 mg, of Cortisone, 200 mg, and of Hydrocortisone, 100 mg. If these drugs are effective after several days, the dose is gradually reduced to a maintenance dose, which is usually one-fourth to one-half the initial dose Since they cause sodium retention and potassium loss, the patient should be placed on a low sodium diet and fruit juices given liberally for their potassium content Potassium also may be given by mouth

Congestive Failure.—Although the superiority of ACTH and Cortisone over salicylates has not been proven in the ordinary case of rheumatic fever, they are very valuable in a number of patients severely ill with congestive failure,[179,344] as the following case demonstrates

A man of 29 with rheumatic pericarditis was in severe left and right heart failure which did not respond at all to the usual therapy Marked tachycardia and gallop rhythm were present After receiving 25 mg of ACTH every six hours for six days, he improved remarkably The daily dose of ACTH was then reduced from 100 to 60 mg, and this was maintained for seven days It was then further reduced to 40 mg This treatment was continued for two more weeks and the patient made an excellent recovery In this patient, heart failure was relieved only when the adrenal cortical hormones were used It was our opinion that without them death would have occurred

The beneficial effect of ACTH and Cortisone in acute rheumatic fever complicated by congestive failure is particularly important since digitalis is often ineffective in this situation[323] and may even be harmful since there is a tendency to push the dosage of digitalis to toxic levels in order to obtain an effect [263] It is, therefore, wiser to depend

upon salt restriction, mercurial diuretics and hormonal therapy in congestive failure before digitalization is attempted. If the failure persists, digitalis should be administered for it may be effective, particularly if atrial fibrillation is present.[323] Its administration should be controlled with particular care to avoid intoxication.

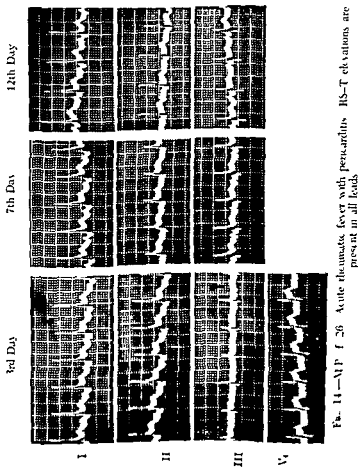


Fig. 14—M P f 26 Acute rheumatic fever with pericarditis. RS-T elevations are present in all leads.

In the usual attack of rheumatic fever, *salicylates* should be given in large daily doses of 3 to 6 gm. This amount is given in divided doses every four hours. Salicylates are quite effective in controlling the fever and joint pains in acute rheumatic fever, and may have a favorable effect upon the exudative phase of the disease, i e, pericardial and joint effusions.[148]

Acute Pericarditis.—Acute pericarditis is common in acute rheumatic fever and may be associated with severe precordial or epigastric pain which is relieved only by morphine It usually develops within a few days after the onset of the attack A friction rub may be heard and, rarely, shock may occur. The electrocardiogram usually presents a typical pattern consisting of RS–T elevation in two or more leads, without Q–waves (Fig 14) and often with subsequent development of T–wave inversion If an effusion accumulates, the rub may disappear and the patient usually becomes more dyspneic and orthopneic Should these symptoms increase and the venous pressure rise, the picture of congestive failure is simulated Tapping of the pericardium is rarely necessary, however, and is required only if cardiac tamponade develops rapidly Usually the fluid is resorbed spontaneously as the acute infection subsides on bed rest and drug therapy In these cases, as in congestive failure, ACTH and Cortisone may be more effective than the salicylates and should be used

In the course of *chronic rheumatic heart disease* with mitral stenosis and atrial fibrillation, atrial thrombi may form and, in rare instances, may be large enough to occlude the valve opening (ball valve thrombus).[93,286] This produces a real emergency since blood is unable to enter the left ventricle and the cardiac output is greatly diminished Cyanosis appears at the extremities of the circulation, i e, the tip of the nose, the lobes of the ears and the fingers and toes, and severe dyspnea, congestive heart failure and shock usually develop. In rare instances the thrombus may

be demonstrated by angiocardiography, a radiolucent area being noted in the atrial chamber. Death may occur suddenly[6] or the patient may live for many years. The treatment is supportive including oxygen and the usual measures employed in congestive failure and shock. Morphine, 15 mg. (¼ gr), may relieve the restlessness. Occasionally, a change in position causes the thrombus to move and relieves the condition We have observed the cyanosis to disappear immediately when the patient sat up and leaned forward. Surgical removal of the thrombus presents technical difficulties but seems feasible if the newer methods developed in cardiac surgery are employed, *i e*, cross circulation, artificial heart or hypothermia

Thrombi in the right auricle[183] may be carried to the lungs, causing pulmonary infarction, and those from the left auricle may be released into the blood stream, resulting in cerebral or peripheral arterial embolization Emboli occur more commonly in isolated mitral stenosis than when it is combined with mitral insufficiency The treatment of these vascular accidents has been discussed in Chapter 3 In peripheral embolization embolectomy is the procedure of choice if the diagnosis is made within several hours

In rheumatic heart disease one embolic episode is apt to be followed by others Therefore, an attempt should be made to prevent a recurrence. This may be done either medically or surgically Medical treatment consists of administering an anticoagulant such as Dicumarol over a number of years[65, 317] We have observed such a patient over three years during which time not a single embolic episode has occurred, whereas she had developed many of these prior to the institution of Dicumarol therapy The patient takes 50 mg of the drug five days a week and her prothrombin time is determined once a month. It is easily controlled in this patient, but others require much closer observation The surgical procedure originally performed for recurrent peripheral embolization was left auricular appen-

dectomy,[31,77,202] but recent studies have demonstrated that thrombi form in the atrial cavities as well as in the appendages and that unilateral resection may not be effective.[163,322] The procedure is reserved for cases in which contraindications to valvulotomy exist.[239]

In recent years the development of mitral valvulotomy or commissurotomy as a safe and effective operative procedure has revolutionized the management of chronic rheumatic valvular disease with mitral stenosis.[133] Many patients with even marked restriction of activity and signs of congestive failure have been restored to relatively good health following operation and are able to work. The mortality rate is now less than 15 per cent.

While there is still no unanimity of opinion as to all the indications for mitral valvulotomy and left auricular resection, the operation should be considered in every patient with mitral stenosis. The following indications are generally accepted (1) symptoms of cardiac insufficiency, e g, increasing dyspnea and fatigue or *attacks of pulmonary edema*, (2) signs of congestive failure, whether mild or severe, (3) auscultatory, roentgenologic, electrocardiographic and vectorcardiographic evidence of mitral stenosis and right ventricular enlargement, (4) increased pressure in the pulmonary artery and right ventricle on catheterization, (5) recurrent *embolic episodes* and (6) recurrent *hemoptysis*

Some physicians perform commissurotomy in all patients with definite mitral stenosis before the advent of symptoms of heart failure and of increased pulmonary artery pressure It must be remembered, however, that many patients with mitral stenosis remain asymptomatic for many years and live out their normal life span Although it is not possible to predict which patients will run such a benign course, it would seem advisable to perform the operation only when there is a specific indication until the results of the procedure have been observed over a longer period of years.

On the other hand, it is important not to delay the operation until the patient is quite ill, since the results are better in patients with mild degrees of failure than in those in advanced failure.

The major contraindications to mitral valvulotomy are the presence of acute rheumatic fever or subacute bacterial endocarditis and significant left ventricular enlargement, whether caused by mitral insufficiency or aortic valve disease. A mild degree of mitral insufficiency or a minimal aortic lesion does not preclude the operation, but the finding of definite left ventricular enlargement on fluoroscopy or of left ventricular hypertrophy in the electrocardiogram makes the case unacceptable One of the major difficulties in this field is the detection of mitral insufficiency in patients with mitral stenosis Experience has shown that the presence of an apical systolic murmur is not in itself a reliable sign of mitral insufficiency, unless it is at least of grade 3 intensity.[159] At operation it has been found that pure mitral stenosis not infrequently exists without insufficiency Yet in one such series[157] a systolic murmur of grade 1 or 2 intensity (rarely 3) was present in 30 per cent of these cases A grade 4 apical systolic murmur indicates definite mitral insufficiency, and in this lesion the murmur usually occupies all of systole and may include the second sound. A number of complicated procedures have been suggested for differentiating mitral stenosis and insufficiency but they have not proven superior to auscultation, fluoroscopy and electrocardiography [2]

Atrial fibrillation and advanced age (over 50) are not contraindications to mitral valvulotomy

While a history of arterial embolic phenomena is sometimes considered a contraindication to mitral commissurotomy, because of the probability of postoperative embolism, our experience and that of others in such cases has been favorable For example, three years ago a woman of 48 with long-standing mitral stenosis and frequent episodes

of paroxysmal atrial fibrillation developed a popliteal embolism. The embolus was removed surgically within three hours with complete restoration of circulation. Six weeks later mitral valvulotomy was performed Post-operatively she developed atrial fibrillation which persisted for 12 days Since then she has been asymptomatic except for intermittent premature beats and occasional brief episodes of atrial fibrillation which are readily controlled with quinidine

We, therefore, advise commissurotomy in patients with a history of embolic episodes. Embolization to the brain during the operation may be prevented by momentarily occluding the left common carotid and the innominate arteries by pressure at the instant of valve fracture [47]

Mitral valvulotomy has a low morbidity and mortality in the hands of an experienced team consisting of surgeon, cardiologist and anesthesiologist working in close cooperation during and after the operation. During the operation it is advisable to follow the rhythm of the heart electrocardiographically in order to detect arrhythmias or cardiac arrest (See Chapter 9) Postoperatively, severe pain in the area of the incision, arrhythmias and peripheral embolism may occur. Precordial pain, dyspnea, tachycardia and fever ("post-commissurotomy syndrome") have been noted during the first three to six weeks after the operation, but they may be delayed and may constitute an emergency.[297] It is not clear whether the attack represents rheumatic reactivation or a pleuro-pericarditis, but the symptoms usually subside after four or five days without specific therapy.

Recently surgical procedures for the correction of aortic stenosis and of aortic and mitral insufficiency have been performed Favorable results have been reported by several groups, but it is still too early for definite evaluation of these operations.[9, 161] Furthermore, double lesions, either of the same valve or of both the mitral and aortic valve, have been corrected at one sitting in some patients However, such a procedure should be undertaken only if it is certain

that both lesions are causing a significant circulatory disturbance For example, when both aortic and mitral stenosis are present, it may be necessary only to correct the mitral lesion to achieve clinical improvement The introduction of the techniques of hypothermia, cross-circulation, and the artificial heart in cardiac surgery has opened untold possibilities in this field, and continued advances in correcting valvular defects in rheumatic heart diseases are inevitable.

Chapter

6

HYPERTENSIVE ENCEPHALOPATHY AND CRISES—PHEOCHROMOCYTOMA

HYPERTENSIVE crises may occur in the course of essential hypertension, particularly in its malignant phase, in acute nephritis and in cases of chronic nephritis with uremia. Severe unremitting headache, nausea and vomiting, paraesthesias, convulsions, blindness, stupor or coma may be observed. In some instances these episodes are terminal and regardless of therapy the patient will not survive. Relief of symptoms is the most that can be expected from treatment. In other instances the crisis is temporary and represents an exacerbation of a disease which may be in its early stages or which may be reversible. This latter group of patients should be treated as quickly and vigorously as possible, for recovery may be followed by many months or years of comfortable living.[232]

The symptoms which occur are most probably secondary to increasing blood pressure and cerebral edema. Relief from these attacks has occasionally been obtained by the intravenous administration of 20 to 40 cc. of a 10 per cent solution (2 to 4 gms.) of magnesium sulfate, or 50 cc. of 50 per cent dextrose or by the withdrawal of spinal fluid. Results with these dehydrating procedures do not compare, however, with the dramatic response noted in some patients when sympathetic blocking or other "antihypertensive" agents are employed. Many of these drugs

have been used to relieve the symptoms of hypertensive encephalopathy and prevent permanent cerebral, renal or ocular damage

Although use of the parenteral Veratrum derivatives (Veriloid and Protoveratrine) may occasionally produce good results,[223 366] most of our own experience has been with the Dibenamine derivatives, Hydrazinophthalazine, (Apresoline) and Hexa- and Pentamethonium.[233] Intravenous Dibenzyline (5 to 1 0 mg /kg given in an infusion of glucose in water over a twenty-to-thirty-minute period) will often produce dramatic relief of headaches and a fall in blood pressure. Mental symptoms may be relieved for several days after one dose of this drug [233] We do not believe, however, that it is the drug of choice since a definite effect is not always obtained, and if a severe, prolonged hypotensive reaction does occur, none of the presently available pressor agents are effective in counteracting the hypotension. Apresoline (20–50 mg intravenously) will also produce a fall in blood pressure in patients with hypertensive encephalopathy but it may aggravate the headache, nausea and vomiting

At the present time we believe that the use of parenteral Hexamethonium (Bistrium) is the most satisfactory method of treating these patients during the acute episode This drug must be given slowly and the dose necessary to produce an effect must be determined in each patient In general, patients with the highest pressures prove to be the most sensitive to drug action It is best to administer the first dose intravenously as an infusion (100 mg of Bistrium in 100 cc of glucose in water given at a rate of approximately 1 cc /minute) Blood pressures should be checked every minute with the patient in a sitting position As soon as a blood pressure fall to the desired level $\frac{(150 \text{ to } 170)}{(100 \text{ to } 110)}$ occurs, the infusion should be stopped and the patient lowered to a recumbent position If this method is followed few hypo-

tensive reactions will occur. The infusion should not be continued until a *normal* blood pressure is obtained since a further lowering of blood pressure may be noted five to ten minutes after the infusion has been stopped. A marked degree of hypotension might thereby be produced if this method were followed. Pressure should be stabilized at between $\frac{150\text{–}170}{100\text{–}110}$. The average dose of Hexamethonium necessary to produce this effect is between 15 to 60 mg, although occasionally 100 to 125 mg may be necessary.

If a reaction does occur the patient should be maintained in a marked Trendelenburg position until the blood pressure returns to more normal levels. It will rarely be necessary to do anything further but if blood pressure remains exceptionally low, small doses (25 to 5 mg) of intravenous neosynephrine will promptly raise the pressure level. This or any pressor drug should be used with care after Hexamethonium since patients "under blockade" are extremely sensitive to them. All patients should remain recumbent or semi-recumbent for at least one and one-half to two hours after the use of Hexamethonium. After the initial intravenous dose, subsequent doses may be given subcutaneously (Approximately 5 to 15 mg more than the effective intravenous dose every three to four hours). Utilizing this method we have never seen a patient whose blood pressure could not be lowered and controlled. This, of course, does not imply that recovery will occur, especially if renal disease is severe, but with effective blood pressure control symptomatic relief may be obtained and further cerebral damage curtailed. Hexamethonium or any of its derivatives should be used with care in patients with renal impairment because of the danger of further reducing renal blood flow and increasing the degree of azotemia.

An example of the above method of therapy of hypertensive encephalopathy is provided by the following case.

A forty-four-year-old negro male with known hypertension of sixteen years' duration began to experience severe headaches, nausea and vomiting His blood pressure varied between 210/130 and 220/150 and fundoscopic examination revealed a Grade IV retinopathy (hemorrhages, exudates, papilledema) Left ventricular hypertrophy was present but renal function was adequate The patient was considered to be a severe hypertensive with encephalopathy Twelve milligrams of Hexamethonium were given as described above. His pressure fell and his headache disappeared within twenty minutes He was maintained on 20 mg. of Hexamethonium subcutaneously on a four-hour schedule for the next twenty-four hours Symptoms cleared The patient was then placed on oral Hexamethonium and Apresoline Headache, nausea and vomiting did not return and papilledema cleared

An excellent symptomatic and blood pressure response has been obtained in other patients but some have progressed to a fatal outcome At postmortem, severe renal disease has been found It is, of course, impossible to do more than alleviate symptoms in these individuals

The use of Arfonad (a Thiophanium derivative and effective ganglionic blocking agent)[278] has been advocated for the treatment of hypertensive crises by some observers This compound lowers blood pressure but has an extremely short duration of action It may be administered in an infusion (1 to 2 mg/cc in 5 per cent dextrose) or as a single intravenous injection 1 to 2 mg/kg Another, more potent, longer acting ganglionic blocking agent, Ansolysen[107,278] (pentapyrrolidinium) is also an effective blood pressure lowering agent Although this drug appears to be superior to Hexamethonium when utilized orally in the long term management of the ambulatory hypertensive patient, its use intravenously in hypertensive encephalopathy would not appear to present any advantages over the use of Hexamethonium It is approximately five times

as potent as Hexamethonium and is administered in doses of 3 to 15 mg. when given parenterally.

If nausea and vomiting prove troublesome during an episode of hypertensive encephalopathy, Thorazine, Dramamine or Marazine should be given immediately One to 2 cc of Thorazine intramuscularly every four hours, and then 25 mg. every four hours by mouth as soon as this is tolerated, will rarely fail to relieve this annoying and potentially dangerous symptom.

There is no longer any reason to be content with overwhelming these patients with sedatives, and allowing the disease to run its course Many can be greatly benefitted by therapy Undoubtedly within the next few years safer and better drugs will be introduced for use in these crises.

Pheochromocytoma.—Pheochromocytoma, a tumor which secretes both epinephrine and norepinephrine, is usually found in the adrenal medulla or the retroperitoneal chromaffin tissue It may cause attacks of severe hypertension with headaches, palpitations, tachycardia, vertigo, abdominal pain, nausea, vomiting and profuse sweating[245] Because of the increased amount of circulating epinephrine in patients with a pheochromocytoma an elevation of the basal metabolic rate sometimes occurs Occasionally glycosuria and an elevated blood sugar are present as a result of an increased glycogen breakdown secondary to epinephrine action The attacks of palpitation, sweating, etc, may be sudden in onset, and occasionally can be induced by palpating the region of the kidneys, although in our experience this is unusual. In many cases of pheochromocytoma, the hypertension is persistent and chronic headaches and continuous sweating are present. The diagnosis of this tumor should be considered in hypertensive patients who perspire profusely or who have an elevated basal metabolic rate, a glycosuria or a marked loss of weight. It may be confirmed by the use of one or several specific tests If the patient is seen during a normotensive phase, the use of

histamine[272] (.025 mg. intravenously) will produce a rise in blood pressure and a reproduction of the acute attack The rise in blood pressure is probably the result of a dilatation of blood vessels in the tumor and/or a direct stimulating effect with a resultant increased outpouring of epinephrine.

Benzodioxane,[120] and Regitine,[85] both of which cause a fall in the blood pressure and bring relief of symptoms as a result of their action in blocking the effects of circulating epinephrine or norepinephrine, are to be used during the hypertensive phase in patients with pheochromocytoma The Regitine test (5 mg intravenously) is a simple, safe office procedure If this test is positive the results should be checked with a Benzodioxane Test (1 mg /10 lbs given slowly intravenously). Reactions (marked elevation of blood pressure or convulsions) occasionally occur with Benzodioxane when the drug is used in patients with hypertension not secondary to pheochromocytoma, and this test should only be performed in the hospital "False positive and negative" results have been reported with all of these agents and several tests should be done to check the diagnosis

Sedation should not be employed for thirty-six hours before the Regitine Test as "False Positive" results are often obtained in patients receiving sedatives Interpretation of any test in the presence of uremia should be guarded Assay of urinary excretion of epinephrine and norepinephrine[119] may eventually prove to be of more value in the diagnosis of this tumor than any of the above tests

Although calcification in a pheochromocytoma is uncommon, its presence in the region of the adrenal gland may suggest the diagnosis in a hypertensive patient with any unusual symptoms.[235] The presence of diffuse electrocardiographic changes (probably as a result of epinephrine effect) in a patient with hypertension should also suggest the diagnosis [279]

Since hypertension secondary to pheochromocytoma is the only type of hypertension that can almost always be cured by surgical intervention, we feel that *all* patients with either fixed or paroxysmal hypertension should be studied for the presence of this tumor. Although the tumor is relatively uncommon the discovery of only an occasional case is extremely gratifying

Acute hypertensive episodes secondary to pheochromocytoma should be treated with intravenous and/or oral Regitine We have also used oral Dibenzyline (10 mg three times daily) to maintain several patients in a normotensive state while they awaited surgical exploration, although we do not feel that preoperative therapy of this type is necessary in most cases Hypertensive attacks that occur as the tumor is palpated during laparotomy usually are transient and no therapy is required If they persist, 5 mg. of intravenous Regitine will control them

If shock occurs after removal of the tumor this can be controlled successfully by the use of a continuous infusion of norepinephrine (Levophed) (4 mg /1000 cc of glucose in water).

Chapter

7

DISSECTING ANEURYSM

DISSECTING aneurysm of the aorta is relatively uncommon, but its diagnosis is important for two reasons (1) if an erroneous diagnosis of acute coronary occlusion or pulmonary infarction is made and anticoagulant therapy is given, the possibility of recovery from a dissecting aneurysm is further reduced, (2) if a method for the surgical treatment of dissecting aneurysms is perfected, early diagnosis will be essential for success. Only a small percentage of the cases is diagnosed ante-mortem, probably because of the failure to suspect the presence of the condition Contrary to general belief, a dissecting aneurysm is not invariably fatal, 10 to 25 per cent of patients have lived for from three months to eight years following its onset [148] The dissection may be acute, lasting only a few hours, and terminate in death as a result of the rupture of the aorta, or it may be subacute, causing repeated bouts of pain for a period of two to five days, and end in recovery

The attack does not appear to be precipitated by unusual exertion, usually occurs in elderly patients with hypertension, and is sudden in onset At least two-thirds of cases occur in males [28] In the younger age group dissecting aneurysm is occasionally associated with coarctation of the aorta and pregnancy Occlusion of a branch of the aorta, *i e*, iliac, intercostal, or coronary, is common There is a sharp, knife-like pain in the chest and/or back, with occasional radiation to the epigastrium, the lower abdomen, the flanks and

the legs. Syncope is noted in 10 per cent of the cases and shock may occur quickly. The patient may writhe in severe pain, but unlike the pain of coronary occlusion this is not "crushing" or "constrictive" and does not require a minute or two to reach its maximum intensity. Various neurologic signs may appear, including paraplegia, which is caused by hemorrhagic infarction of the spinal cord.[202] An aortic diastolic murmur is heard in many cases. Electrocardiographic evidence of left ventricular "strain" or coronary insufficiency may appear, or of coronary occlusion if the dissection occludes a coronary artery. A coronary occlusion secondary to a dissecting aneurysm may sometimes be differentiated from the ordinary type of coronary occlusion by the presence of pain in the upper or lower back, the lower abdomen or the legs, by the sudden appearance of a diastolic murmur, or by the presence of neurologic changes, especially "sensory loss" in the lower extremities. If a pleural or pericardial effusion or hemmorrhage into the wall of the aortic arch occurs, a widened mediastinum may be detected on fluoroscopy or x-ray. This procedure should be carried out with great caution and actually should not be used if the diagnosis is fairly well established from other findings. The diagnosis should be considered in any patient with hypertension who suddenly develops severe knife-like pain in the chest, back, epigastric region or legs, and in whom a diastolic murmur suddenly appears.

A case in which the correct diagnosis was suggested during life was that of a hypertensive man of forty-two who developed episodes of severe substernal pain and shock with apparent complete recovery between attacks. The electrocardiogram showed the deep Q-waves and RS-T elevations characteristic of coronary occlusion. On the third day, during one of his attacks, the heart sounds suddenly became faint and the area of cardiac dullness increased. A pericardial tap revealed hemopericardium and a diagnosis of dissecting aneurysm was made. He died almost immediately

and postmortem examination disclosed a dissection involving a coronary artery.

Many times, however, the history and findings are completely atypical and a correct diagnosis cannot be made For example A sixty-three-year-old white male complained of sudden, severe, intermittent pain in the left lower quadrant He had experienced mild pain in that region eight months before for a period of four or five days, but the pain had not recurred until the present admission Examination revealed an ill-defined mass in the left lower quadrant. His blood pressure was 170/100 and no murmurs were heard A diagnosis of carcinoma of the colon or diverticulitis was made Several days later the patient was found to be quite pale and the mass appeared to be larger Twenty-four hours later he died suddenly Necropsy showed evidence of dissection of the aorta from the thoracic to the abdominal portion with rupture of the abdominal aorta and retroperitoneal hemorrhage.

When the presence of a dissecting aneurysm is suspected, the patient should be put to bed immediately Repeated doses of morphine should be given if necessary to attain complete sedation He should be kept in bed for at least three weeks and then should gradually be permitted to walk Anticoagulants should not be used. If an accurate diagnosis is made, and if treatment is instituted early, a much larger percentage of cures may be effected. Since the pain pattern in many cases of dissecting aneurysm may be intermittent, with one or many hours of "quiescence" in between periods of pain, the prognosis should be guarded until at least one week after all symptoms have disappeared

In view of the tremendous advances in vascular surgery it is not unlikely that a procedure will be developed to rechannel the blood in the dissected coats of the aorta into the lumen of the vessel A prerequisite to this, however, is the discovery of methods to detect the site and path of the dissection.

Chapter

8

TRAUMATIC HEART DISEASE

THE heart may be injured directly by penetrating bullet or knife wounds or indirectly by severe blows to the chest[11,18]

The diagnosis of a *penetrating wound of the heart* is simple if external evidence of the injury is present Occasionally, however, a bullet or a needle which had entered the body at some remote point may be carried to the heart through the veins[131] and produce cardiac damage. In these cases the diagnosis is often difficult. If a patient with a recent penetrating injury of the chest wall presents evidence of blood loss, congestive heart failure or shock, trauma of the heart should be suspected The most common result of such trauma is hemorrhage into the pericardial sac or laceration of the myocardium with infarction In rare instances valvular rupture may occur When hemopericardium develops, fluoroscopy or *x*-ray may show evidence of a widened cardiac shadow with diminished pulsations or the electrocardiogram alone may show characteristic RS–T elevations. Occasionally findings in such cases are similar to those seen in myocardial infarction If there is evidence of increasing hemopericardium and cardiac tamponade, *i.e*, shock, with a weak thready pulse and drop in blood pressure (low cardiac output), or congestive heart failure, a pericardial tap should be performed immediately and as much blood as possible aspirated[284] If blood reaccumulates, or if the symptoms persist or recur, a severe

myocardial laceration has occurred and surgical repair should be carried out immediately

Shock should be treated as efficiently as possible before and during the operation. The Trendelenburg position, frequent transfusions of blood (plasma or a volume expander such as dextran if blood is not available), and the use of morphine or Demerol for pain and apprehension often help the patient to surmount the crisis until the wound is repaired Despite the presence of cardiac tamponade the cardiac output may be increased and the patient's condition improved by these measures [325]

Excellent reviews of the technique of repairing cardiac lacerations or removing foreign bodies from the heart have been written [18,132] These surgical procedures need not be discussed here. Complications such as cardiac arrest encountered during operation are discussed in Chapter 9 In experienced hands, the operative mortality rate is 25 to 30 per cent [31] The site repaired usually heals and a firm scar develops. Despite the fact that a major coronary artery is often ligated, infarction does not always occur, and even if it does, cardiac function is usually good [142] A case seen by us demonstrated this finding W C, a thirty-five-year-old laborer was stabbed in the region of the heart with a long knife two hours prior to admission There was profuse hemorrhage but the patient walked several blocks to the hospital He complained of pain in the chest but was neither dyspneic nor cyanotic The blood pressure was 100/80 Heart sounds were distant and a pericardial rub was heard which soon disappeared An *x*-ray of the chest and an electrocardiogram were negative In view of the profuse bleeding, an exploratory operation was performed A laceration of the parietal pericardium, with a moderate hemopericardium and an insignificant stab wound of the anterior surface of the heart were found Upon gentle manipulation the occluding blood clot was dislodged and free bleeding occurred, this could be controlled only by the insertion of

three sutures, two of which entered the chamber. Following the operation, the electrocardiogram showed RS–T elevations followed by T-wave inversions in the standard leads (chest leads were not taken because of the chest strapping), *i.e.*, the typical serial changes of acute pericarditis. In addition, a Q-wave appeared in lead II, this produced a W-shaped QRS which was still present a year later when the T-waves in the standard leads had returned to normal. The alteration in the QRS complex was probably produced by ligation of a coronary artery during the operation, but the patient made an excellent functional recovery.

In some cases a bullet or shrapnel fragment may penetrate the chest and lodge in the heart without producing any cardiac symptoms. The fragment may be visualized by x-ray or fluoroscopy. It is best not to remove the foreign body unless a pericardial reaction occurs. We have observed two cases of interventricular septal defect secondary to bullet wounds where the fragment had penetrated the septum from left to right and lodged in the right ventricle. Both patients did well without surgical removal of the bullet.

Nonpenetrating chest injuries may produce myocardial contusion with signs and symptoms that are difficult to distinguish from those noted in spontaneous coronary occlusion or coronary insufficiency. The causal relationship between trauma and myocardial damage is frequently difficult to establish. As a rule, only a very severe blow to the chest wall produces a detectable cardiac injury. Many boxers and victims of accidents who sustain injuries to the chest show no anatomical or electrocardiographic evidence of myocardial damage.[53, 123]

Many cases of alleged traumatic coronary occlusion reported in the literature probably represent instances of coincidental occurrence of coronary occlusion and trauma. The electrocardiograms which have been reported in a large number of these patients as showing an occlusion

actually show only ST and T-wave changes which occur in coronary insufficiency and not in occlusion [234, 124] In some instances a careful history will elicit the fact that the precordial pain preceded the accident Although we are certain that episodes of coronary insufficiency may be precipitated by effort or trauma, we believe that the occurrence of coronary occlusion is coincidental with extreme physical exertion and that the occlusion had occurred prior to the injury [208, 209]

Trauma to the chest wall occasionally may produce subendocardial tears and myocardial contusions in otherwise normal hearts [145] All cases of so-called "steering wheel" accidents should be carefully observed for several days in a search for electrocardiographic or clinical evidence of heart damage, even in the absence of rib fracture or severe external injury [180] These patients may show various arrhythmias without other changes for several days following the accident We recently observed a forty-year-old man with a persistent rapid atrial fibrillation for over two weeks following a severe "steering wheel" accident. Hemopericardium was present and drug therapy was ineffective in controlling the arrhythmia Fortunately, this eventually subsided spontaneously All cases with a definite history of severe chest trauma that develop precordial pain or discomfort at the time of the injury should be suspected of having sustained a myocardial contusion, the patients should, therefore, be put to bed and given adequate sedation

The following criteria are helpful in determining whether the cardiac damage was caused by a specific trauma [180] The decision must be made on the basis of the facts in each case, but, in general, we require the presence of two or more of these criteria for causal relationship

1. Significant electrocardiographic changes must be present.
2. Cardiac enlargement unexplained by pre-existent cardiac disease or hypertension must appear.

3 Abnormal rhythms (excluding premature beats unless they are accompanied by other electrocardiographic changes) must occur

4 A pericardial friction rub must be heard, or evidence of effusion found

5 Congestive heart failure, precipitated by the blow or strain, must develop

6 Clinical signs and laboratory evidence of coronary insufficiency and/or myocardial infarction must become manifest within twenty-four hours following the incident

Patients with myocardial contusion should be treated in the same manner as those with nontraumatic coronary insufficiency or occlusion with the exception that anticoagulant drugs should be withheld because of the frequent occurrence of pericardial hemorrhage. If hemopericardium does occur, the blood should be repeatedly aspirated if necessary

Rupture of the heart occurs in a few of these cases within ten days to two weeks after the trauma, but if the patient is put to bed as soon as symptoms appear, the incidence of this fatal complication may be reduced.

Many cases of traumatic myocardial damage recover completely after three to five weeks of bed rest and show no permanent clinical or electrocardiographic evidence of heart disease

Chapter

9

SURGICAL EMERGENCIES IN CARDIOVASCULAR DISEASE: THEIR PREVENTION AND TREATMENT

Surgery in the Cardiac Patient.—Recent advances in surgical techniques and anesthetic management have significantly reduced the mortality and morbidity associated with surgery in the patient with heart disease. The necessity for operative intervention, however, in individuals with cardiovascular disorders has also greatly increased with the increase in the aged population, and there is an even greater *need for the careful medical supervision of such patients* in order to prevent the development of postoperative acute congestive failure, coronary insufficiency, tachycardias and pulmonary embolism.

Most patients with heart disease tolerate an operation well, the exceptions being those who are in intractable failure or are recovering from a recent myocardial infarction. Serious complications may not develop even in these *patients if the pre- and postoperative treatment is properly* administered.

Age should not be a deterring factor in patients who require surgery.[212] In fact, many elderly patients with heart disease and severe cardiac disability are occasionally improved by the surgical removal of a "focus of irritation." For example: M.S., a fifty-nine-year-old housewife, who had been an invalid because of severe recurrent attacks

of angina pectoris, also experienced frequent biliary colic. The surgeons were hesitant about operating on her because of her cardiac condition but they were finally prevailed upon to do so She tolerated the operation well and has remained practically free of her anginal attacks for many years. Another example was M R, a sixty-year-old woman with gall bladder disease who suffered an acute posterior wall infarction Her convalescence was marked by repeated attacks of severe biliary colic A cholecystectomy was performed one month after the occlusion had occurred Her postoperative course was uneventful and since then she has not complained of pain It is usually advisable to wait two to three months after the electrocardiogram has stabilized following a myocardial infarction before surgery is performed, unless, of course, an acute situation makes immediate intervention a necessity.

In the presence of *heart failure* operation should be performed only when it is urgently needed and only after careful preparation if time permits. Even when proper preparation is not possible, the results have often been good When congestive failure exists, rapid intravenous digitalization should be carried out and mercurial diuretics given In patients with rheumatic heart disease and atrial fibrillation the rate should be slowed by intravenous digitalis therapy before surgery is attempted. Persons with compensated heart disease may be expected to withstand operative procedures as well as those whose hearts are normal if certain precautions are taken. Special attention should be paid to the amount of fluids and sodium given pre- and postoperatively, and an adequate quantity of oxygen should be administered during the operation. The administration of large quantities of intravenous saline after an operative procedure should be avoided in cardiac patients in order to prevent pulmonary edema and congestive heart failure.

In patients with coronary artery disease particular care should be exercised to avoid hypoxia, especially during the induction of anesthesia, and *hypotension* during the course of the operation. Spinal anesthesia has usually been considered dangerous for patients with coronary artery disease or severe hypertension, but we have found it effective and safe for operations on the lower abdomen or pelvis. Intramuscular methoxamine (Vasoxyl), neosynephrine or ephedrine may be given prophylactically to prevent a precipitous fall in blood pressure during spinal anesthesia and intravenous Vasoxyl (5 mg.) or neosynephrine (.5 to 1.0 mg.) should be available for immediate use if hypotension should occur. Norepinephrin (Levophed), 4 mg. in 1000 cc. of glucose, is also effective in maintaining blood pressure during surgery if hypotension is not secondary to blood loss. *In the latter case blood should be given as soon as possible.*

Although it was formerly believed that local or regional anesthesias were to be preferred in patients with coronary artery disease, experience has demonstrated that general anesthetics are more satisfactory, provided that adequate oxygenation and ventilation are maintained at all times. Apprehension and some degree of pain which are often associated with local anesthetics are thereby eliminated. If a general anesthetic is used, ether is preferred or a thiopental induction followed by oxygen and cyclopropane may be used. Since the latter may induce ventricular arrhythmias,[161] quinidine, two doses of 6 gr. (.4 gm.), or Pronestyl[164] (1.0 to 1.5 gm.) should be given orally before the operation, particularly in patients with a history of arrhythmias. These agents markedly reduce the incidence of tachycardias that occur during surgical procedures. If atrial tachycardia, flutter or fibrillation develops, quinidine should be given intramuscularly. If a ventricular arrhythmia sets in despite these prophylactic measures, Pronestyl may be injected intravenously, but slowly and cautiously with electrocardiographic control.

The incidence of postoperative thromboembolism and pulmonary infarction is higher in cardiac than in noncardiac patients and, in fact, probably accounts for a higher percentage of deaths in these patients than any other single complication. The most important factor in preventing these complications is early ambulation, particularly in the obese. The patient should also be instructed to turn in bed as soon as possible, to move his legs within several hours after the operation, and to avoid straining at stool. Should pulmonary infarction occur, despite these measures treatment is given as outlined in Chapter 3.

During the course of cardiac surgery for the correction of either congenital or acquired valvular defects many unusual arrhythmias may occur, especially during the period of valve manipulation or "fracture." The majority of these arrhythmias are supraventricular and cease spontaneously without the use of drugs, the incidence of these arrhythmias cannot be reduced by the use of preoperative Pronestyl or quinidine. If frequent ventricular premature beats or aberrant ventricular beats occur, or if ventricular tachycardia is noted during heart manipulation, the surgeon should immediately stop all surgery for a short time and the anesthesiologist should lighten the depth of anesthesia and increase the ventilatory exchange as well as oxygenation. It is equally as important to remove excesss carbon dioxide as to provide adequate oxygen. Usually ventricular arrhythmias that occur during cardiac surgery will respond without further therapy. The situation in these instances, where the arrhythmia is due to direct manipulation of the heart, is different from those in which surgery in a remote portion of the body is being performed. If ventricular tachycardia persists after manipulation has been stopped, intravenous Pronestyl should be given. If cardiac arrest or ventricular fibrillation occurs, it should be treated as outlined below.

Cardiac Arrest.—Cardiac arrest may occur during the course of an operative procedure in both normal and cardiac patients. In most instances it is due to an overdose of anesthetic agent. However, it may be caused by marked vagal stimulation during the operation and can be prevented in some cases by the intravenous administration of atropine, 6 mg. (1/100 gr.), sixty minutes before surgery, or 3 mg. (1/150 gr.) intramuscularly thirty minutes prior to operation.[162] Cardiac arrest occurs in operations on the chest more often than in abdominal or pelvic surgery. When it does occur, the instantaneous execution of a well-planned course of treatment is essential to save the patient's life.[160]

A sixteen-year-old boy, who was operated upon for atelectasis of the left lung secondary to fibrosarcoma of the bronchus, furnishes a dramatic example of the success of cardiac resuscitation, even after a forty-minute period of cardiac arrest.* He received cyclopropane and ether at 8.10 A.M., at 8.25 A.M., an oral endotracheal tube was introduced. At 8.27, the left hemithorax was entered. Sixty mg. of procaine hydrochloride were injected into the tubing of an intravenous drip. The pulmonary artery was ligated at 9.05, when cardiac arrest occurred. Artificial respiration was begun immediately by intermittent manual compression of the breathing bag of the anesthetic apparatus. Simultaneously, manual compression of the heart was started at a rate of 50 per minute. At 9.10, a mixture of 80 mg. of procaine and 1 mg. of epinephrine was injected into the left ventricular cavity. At 9.25, 60 mg. of procaine and 5 mg. of epinephrine were given, and at 9.30, 80 mg. more of procaine were injected. Cardiac action did not return. At 9.45, the pericardium was grasped with a hemostat, preparatory to incision. At that moment the heart suddenly beat violently and normal pulsation and respiration began. The pneumonectomy was completed without mishap. On the

*This case is described with the permission of the operating surgeon, Dr. Arthur S. W. Touroff.[313]

The incidence of postoperative thromboembolism and pulmonary infarction is higher in cardiac than in noncardiac patients and, in fact, probably accounts for a higher percentage of deaths in these patients than any other single complication. The most important factor in preventing these complications is early ambulation, particularly in the obese. The patient should also be instructed to turn in bed as soon as possible, to move his legs within several hours after the operation, and to avoid straining at stool Should pulmonary infarction occur, despite these measures treatment is given as outlined in Chapter 3.

During the course of cardiac surgery for the correction of either congenital or acquired valvular defects many unusual arrhythmias may occur, especially during the period of valve manipulation or "fracture" The majority of these arrhythmias are supraventricular and cease spontaneously without the use of drugs, the incidence of these arrhythmias cannot be reduced by the use of preoperative Pronestyl or quinidine If frequent ventricular premature beats or aberrant ventricular beats occur, or if ventricular tachycardia is noted during heart manipulation, the surgeon should immediately stop all surgery for a short time and the anesthesiologist should lighten the depth of anesthesia and increase the ventilatory exchange as well as oxygenation It is equally as important to remove excesss carbon dioxide as to provide adequate oxygen. Usually ventricular arrhythmias that occur during cardiac surgery will respond without further therapy. The situation in these instances, where the arrhythmia is due to direct manipulation of the heart, is different from those in which surgery in a remote portion of the body is being performed. If ventricular tachycardia persists after manipulation has been stopped, intravenous Pronestyl should be given. If cardiac arrest or ventricular fibrillation occurs, it should be treated as outlined below

If respirations have ceased, artificial respiration should be started simultaneously with the exposure of the heart. If possible, an endotracheal tube should be inserted and the lungs inflated and deflated by mechanical means This is by far the most efficient method of supplying oxygen[59] If endotracheal tubes are not available, however, the resumption of respiration may be effected by mouth to mouth breathing, alternating manual pressure and release of the costal cage, or the use of a tight-fitting face mask, pressure being applied intermittently to the breathing bag When the latter method is used there is real danger of forcing air into the stomach and causing marked gastric dilatation.[340] One hundred per cent oxygen should be given and CO_2 mixtures should be avoided since the patient already has accumulated an excessive amount of CO_2 in the tissues Adequate oxygenation of the brain and other organs may be maintained by use of any one of the above procedures until spontaneous respiration and circulation are resumed

When hemorrhage has occurred and the blood volume is markedly decreased, intra-arterial transfusions of blood should be given at the rate of 150 to 200 cc /minute These transfusions are given at a pressure higher than the systolic blood pressure.

In many cases, patients who had apparently expired will be completely revived and will recover with no ill effects if the suggested treatment is undertaken promptly. If the surgeon is properly equipped and psychologically ready for this emergency, good results may be expected Unfortunately, there is often a delay before adequate therapy is started, and although the patient survives, extensive cerebral damage from prolonged anoxia has occurred and the patient remains a neuropsychiatric cripple[100]

Resuscitation of patients who develop cardiac arrest while on the wards or at home is rarely successful because of the delays that are of necessity encountered in these situations Our own experience has indicated that cardiac compression

should never be attempted except under operating room conditions where speedy action is possible. In other situations the use of intracardiac Adrenalin or vigorous thumping on the chest as outlined in Chapter 1 will produce results comparable to those obtained by "slashing open" the chest and massaging the heart.

BIBLIOGRAPHY

1. ABBOTT, K H Acetylcholine in Paroxysmal Tachycardia, J A M A, *113*, 1243, 1939
2. ABELMAN, W H, ELLIS, L B, and HARKEN, D E The Diagnosis of Mitral Regurgitation An Evaluation of Clinical Criteria, Fluoroscopy, Phonocardiogram, Auricular Esophagram and Electrokymogram Am J Med, *15*, 5, 1953
3. ALTANA, G Singular Electrocardiographic Picture Caused by Quinidine, Folia Cardiol, *8*, 189 1949
4. ANREP, G V, BARSOUM, G S, KENAWY, M R, and MISRAHY, J Ammi Visnaga in the Treatment of the Anginal Syndrome, Brit Heart J, *8*, 171, 1946
5. ARMBRUST, C A, and LEVINE, S A Paroxysmal Ventricular Tachycardia A Study of One Hundred and Seven Cases, Circulation, *1*, 28, 1950
6. ARONSTEIN, C G, and NEUMAN, L Ball Thrombus of Heart Report of Case With Review of Literature, Arch Path, *27*, 907, 1939
7. ASTWOOD, E. B, and VANDERLAAN, W P Treatment of Hyperthyroidism With Propylthiouracil, Ann Int Med, *25*, 813, 1946
8. BAKOS, A C P, and ASKEY, J M Fever Due to Procaine Amide Hydrochloride Therapy, J A M A, *149*, 1393, 1952
9. BAILEY, C P, BOLTON, H E, JAMISON, W. L, and NICHOLS, H T. Commissurotomy for Rheumatic Aortic Stenosis I Surgery Circulation *9*, 22, 1954
10. BARACH, A L, and MARTIN, J Effect of Inhalation of Oxygen Under Positive Pressure on Pulmonary Congestion and Edema, J Clin Invest, *15*, 466, 1936
11. BARBER, H. Trauma of Heart, Brit M J, *1*, 433, 1938
12. BARKER, N W, HINES, E A, KVALE, W. F, and ALLEN, E. V Dicoumarol Its Action, Clinical Use and Effectiveness as an Anticoagulant Drug, Am J Med, *3*, 637, 1947
13. BARONOFSKY, D, and SKINNER, A Ligation of Left Auricular Appendage for Recurrent Embolism, Surg, *27*, 848, 1950
14. BARROW, J G Treatment of Paroxysmal Supraventricular Tachycardia with Lanatoside C., Ann Int. Med, *32*, 116, 1950
15. BATTERMAN, R C, and DEGRAFF, A C: Comparative Study on Use of Purified Digitalis Glycosides, Digoxin, Digitoxin and Lanatoside C for the Management of Ambulatory Patients with Congestive Heart Failure, Am Heart J, *34*, 663, 1947

16 BATTERMAN, R C, DEGRAFF, A C GUTNER, L. B, ROSE, O A, and LHOWE, J Studies with Gitalin (Amorphous) for the Treatment of Patients with Congestive Heart Failure, Am Heart J, *42*, 292, 1951
17 BATTERMAN, R C, UNTERMAN, D, and DEGRAFF, A C The Subcutaneous Administration of Mercaptomerin (Thiomerin) Effective Mercurial Diuretic for Treatment of Congestive Heart Failure, J A M A, *140*, 1268, 1949
18 BECK, C S Further Observations on Stab Wounds of Heart, Ann Surg, *115*, 698, 1942
19 BECK, C S STANTON, E, BUTINCHOK, W, and LEITER, E Revascularization of Heart by Graft of Systemic Artery into Coronary Sinus, J A M A, *137*, 436, 1948
20. BECK, C S. Resuscitation of Cardiac Standstill and Ventricular Fibrillation Occurring During Operation, Am J Surg *54*, 273, 1941
21 BECK, C S, PRITCHARD, W H, and FEIL, H Ventricular Fibrillation of Long Duration Abolished by Electric Shock J A M A, *135*, 985, 1947
22 BELL, G O, BRADLEY, R B, and HURXTHAL, L M Paroxysmal Tachycardia, Experiences with Massive Doses of Quinidine Intravenously in a Refractory Case, Circulation, *1*, 939, 1950
23 BELLET, S Clinical Disorders of the Heart Beat Lea & Febiger, 1953 Phila, p 7
24 ——— p 130
25 ——— p 157
26 BELLET, S, and NADLER, C S Use of Quinidine Sulfate in the Treatment of Hiccup, Am J of Med Sc, *216*, 680, 1948
27 BERCU, B A, ROKOW, S N, and MASSIE, E An Antidiuretic Substance in the Urine of Patients with Cardiac Failure, Proc Am Heart Assn, June, 1949
28 BERESFORD, O D The Clinical Diagnosis of Dissecting Aneurysm of the Aorta Brit Med J, *4728*, 397, 1951
29 BERMAN, E F, and AKMAN, L C Intra-arterial Infusion in the Treatment of Shock Resulting from Coronary Occlusion Am Heart J, *43*, 264, 1952
30 BERNSTEIN, M, LEWINN, E B, and SIMKINS, S Heart Disease and Liver Function, J Lab and Clin Med, *28*, I, 1942
31 BIGGER, I A Heart Wounds. Report of 17 Patients Operated Upon in Medical College of Virginia Hospitals and Discussion of Treatment and Prognosis, J. Thoracic Surg, *8*, 239, 1939
32. BLAUSTEIN, A. SHNAYERSON, N, and WALLACH, R Clinical Use of a New Anticoagulant, Phenyl-indandione. Am. J Med. *14*, 704, 1953
33. BLOOMFIELD, A L. Treatment of Auricular Flutter with Digitalis, Editorial, Am J Med, *7*, 437, 1949.

34. Blumgart, H L The Reaction to Exercise of the Heart Affected by Auricular Fibrillation, Heart, *11*, 49, 1924
35 Blumgart, H L, Levine, S A, and Berlin, D D Congestive Heart Failure and Angina Pectoris The Therapeutic Effect of Thyroidectomy on Patients Without Clinical or Pathologic Evidence of Thyroid Toxicity, Arch Int Med, *51*, 866, 1933
36 Blumgart, H L, Freedberg, A S, and Kurland, G J The Treatment of Incapacitated Euthyroid Cardiac Patients with Radioactive Iodine Summary of Results in Treatment of 1,070 Patients with Angina Pectoris or Congestive Failure, *J A M A*, *157*, *1*, *1955*
37. Bolton, H E Delmonico J E, and Bailey, C P Prevention of Cerebral Embolism During Mitral Commissurotomy Results in 433 Consecutive Cases Ann Int Med, *41*, 272, 1954
38 Borg, J F Treatment of Edema with Orally Administered Mercurial Diuretic, Am Heart J, *24*, 397, 1942
39 Boyd, L J, and Scherf, D Magnesium Sulfate in Paroxysmal Tachycardia, Am J M Sc, *206*, 43, 1943
40 Bradbury, S, and Eggleston, C Postural Hypotension, Am Heart J, *1*, 73, 1925
41 Brannon, E S Hemiplegia Following Carotid Sinus Stimulation, Case Report, Am Heart J, *36*, 299, 1948
42 Brannon, E S, Stead, E A, Jr, Warren, J V, and Merrill, A J Hemodynamics of Acute Hemorrhage in Man, Am Heart J, *31*, 407 1946
43 Brill, I C Congestive Heart Failure Arising from Uncontrolled Auricular Fibrillation in the Otherwise Normal Heart, (Follow-up Notes on Previously Reported Case), Am J Med, *2*, 544, 1947
44 Brill, I C, and Meissner, W A Role of Coronary Artery Disease in Etiology of Auricular Fibrillation, Ann Int Med, *14*, 1341, 1941
45 Brofman, B L, Hellerstein, H K, and Caskey, W H Mephentermine—An Effective Pressor Amine Clinical and Laboratory Observations Am Heart J, *44*, 405, 1952
46 Burchell, H B, Adjustments in Coronary Circulation after Experimental Coronary Occlusion with Particular Reference to Vascularization of Pericardial Adhesions Arch. Int Med, *65*, 240, 1940
47 Burke, G E, and Wright, I S Tromexan—3,3' Carboxymethylenebis (4-Hydroxycoumarin Ethyl-Ester) Experimental and Clinical Properties, Cir, *3*, 164, 1951
48 Burnam, J F, Hickman, J B, and Stead, E A, Jr Hyperventilation in Postural Hypotension, Circulation, 10, 362, 1954.

49 Burstein, C Treatment of Acute Arrhythmias During Anesthesia by Intravenous Procaine, Anesthesiology, *7*, 113, 1946
50 Burwell, W B, and Hendrix, J P Digitalis Poisoning, Am J Med, *8*, 640, 1950
51. Burwell, C S, and Dexter, L Beri-beri Heart Disease, Tr A Amer Physicians, *60*, 59, 1947
52 Butterworth, J S, and Poindexter, C A The Esophageal Electrocardiogram in Arrhythmias and Tachycardias, Am Heart J, *32*, 681, 1946
53 ——— Electrocardiographic Study of the Effects of Boxing, Am Heart J, *23*, 59, 1942
54 Citril, Y, and Lyons, R H Diuretic Potency of a New Organic Mercurial, C. T 464 (Dicurin) New York State J Med, *54*, 1359, 1954
55 Cohen, S M Edholm, E G, Howarth, S, McMichael, J, and Sharpey-Schafer, E P Cardiac Output and Peripheral Blood Flow in Arteriovenous Aneurysm, Clin Sc, *7*, 35, 1948
56 Cohn, A E and Steward, H J Evidence That Digitalis Influences Contraction of the Heart in Man, J Clin Invest, *1*, 97, 1924
57 Comeau, W J The Mechanism of Syncopal Attacks Associated with Paroxysmal Auricular Fibrillation, New England J Med *227*, 134, 1942
58 Conn, J W. The Diagnosis and Management of Spontaneous Hypoglycemia, J A M A, *134*, 130, 1947
59 Cook, L Recovery After Massage of the Heart, British Med J *2*, 1118, 1926
60 Cookson, H Aetiology and Prognosis of Auricular Fibrillation, Quart, J Med, *23*, 309, 1930
61 Cornell Conferences on Therapy. Management of Disorders of Cardiac Rhythm Am J Med, *5*, 110, 1948
62 ——— Use of Mercurial Diuretics, New York State J Med *46*, 62, 1946
63 Cossion, T Ligation of the Vena Cava in the Treatment of Heart Failure, Am Heart J, *43*, 97, 1952
64 Cournand, André A Discussion of the Concept of Cardiac Failure in the Light of Recent Physiologic Studies in Man Ann Int Med, *37*, 649, 1952
65 Cosgriff, S W Chronic Anticoagulant Therapy in Recurrent Embolism of Cardiac Origin, Ann Int Med, *38*, 278, 1953.
66 Cutts, F B, and Rapoport, B Routine Use of Quinidine in Acute Myocardial Infarction, New England J. Med, *247*, 81, 1952
67. Dack, S, Master, A. M, Horn, H, Grishman, A, and Field, L. Acute Coronary Insufficiency Due to Pulmonary Embolism, Am J Med, *7*, 464, 1949

68 DAVIES, D T, MANSELL, H E and O SHAUGHNESSY L Surgical Treatment of Angina Pectoris and Allied Conditions Lancet, *1*, 1, 1938
69 DECHARD, G. M, JR, and HERMANN, G R Association of Paroxysmal Atrial Tachycardia with Atrial Flutter or Fibrillation, Am Heart J, *28*, 457, 1944
70. DEGRAFF, A. C Clinical Comparison of Cardiac Glycosides, New York State J Med, *46*, 1803, 1946
71. DEGRAFF, A C, and BATTERMAN, R C Recent Advances in Digitalis Therapy with Particular Attention to the Use of Pure Glycosides, M. Clin North America, *26*, 929, 1942
72 DIMITROFF, S P, GRIFFITH, G C, THORNER, M C, and WALKER, J Clinical Evaluation of Gitalin in the Treatment of Congestive Heart Failure, Ann Int Med, *39*, 1189, 1953
73 DETRICK, J E, WHEDON, G D, and SHAW, E Effects of Immobilization upon Various Metabolic and Physiological Functions of Normal Men, Am J Med, *4*, 3, 1948
74 DOCK, W, and TAINTER, M L. The Circulatory Changes After Full Therapeutic Doses of Digitalis with a Critical Discussion of Views on Cardiac Output, J Clin Investigation, *8*, 467, 1930
75 DOCK, W. Sodium Depletion as a Therapeutic Procedure The Value of Ion Exchange Resins in Withdrawing Sodium from the Body, Tr A Am Physicians, *59*, 282, 1946
76 DOCK, W · Evil Sequelae of Complete Bed Rest, J A M A, *125*, 1083, 1944
77 ——— (quoted in reference 165)
78 EDHOLM, O G, HOWARTH, S, and MCMICHAEL, J Heart Failure and Bone Blood Flow in Osteitis Deformans, Clin Sc, *5*, 249, 1945
79 EDHOLM, O G Effect of Gravity on the Blood Pressure of the Cat, J. Physiol, *98*, 79, 1940
80 EGGLESTON, C: Administration of Digitalis by "Eggleston" Method, J A M A, *74*, 733, 1920
81 EICHNA, L W and TAUBE, H Effect of Intravenously Administered Digoxin and Ouabain on Systemic Venous Pressure of Patients with Congestive Heart Failure, Am Heart J, *27*, 641, 1944
82 EICHNA, L W, TAUBE, H, and DEGRAFF, A C · Serial Determinations of Cardiac Output (Ballistocardiogram) and Electrocardiogram in Normal Man After Intravenous Administration of Purified Cardiac Glycosides, J Pharmacol and Exper. Therap, *78*, 22, 1943
83. ELKINGTON, J. R, SQUIRES, R D, and LINCENSMITH, W C · Cation Exchange Resins in the Treatment of Congestive Heart Failure. Circulation, *5*, 842, 1952.

84. Ellis, L B, and Haynes, F. W. Postural Hypotension With Particular Reference to its Occurrence in Disease of the Central Nervous System, Arch. Int Med, *58*, 773, 1936
85. Emlet, J R, Grimson, K S, Bell, D M, and Oracin, E S Use of Piperoxan and Regitine as Routine Tests in Patients with Hypertension, J A M A., *146*, 1383, 1951.
86 Engel, G L Mechanism of Fainting, J of Mt Sinai Hosp, *12*, 170, 1945
87. Enselberg, C D, Simmons, H G, and Mintz, A A Effects of Potassium Upon the Heart with Special Reference to Possibility of Treatment of Toxic Arrhythmias Due to Digitalis, Am Heart J, *39*, 713, 1950
88 Epstein, F H., and Relman, A Transfusion Treatment of Shock Due to Myocardial Infarction, New England J Med, *241*, 889, 1949
89 Ernstene, A C Cardiovascular Complications of Hyperthyroidism, Am J M Sc, *195*, 248, 1938
90 Evans, J A Poppen, J. L, and Tobias, J. B Relief of Angina Pectoris by Sympathectomy, J A M A, *144*, 1432, 1950
91 Evans, W Unity of Paroxysmal Tachycardia and Auricular Flutter, Brit Heart J, *6*, 221, 1944
92 Evans, W, Dick, P, and Evans, B Rapid Digitalization, Brit Heart J, *10*, 103, 1948
93 Evans, W, and Benson, R Mass Thrombus of Left Auricle, Brit Heart J, *10*, 39, 1948
94 Fauteux, M J Cardiac Resuscitation, Thoracic Surg, *16*, 623, 1947
95 Fauteux, M J Experimental Study of the Surgical Treatment of Coronary Disease, Surg Gynec and Obst, *71*, 151, 1940
96 Feil, H S, and Gilder, M D The Regularity of Simple Paroxysmal Tachycardia, Lond Heart, *8*, 1, 1921
97 Ferrer, M I, Harvey, R. M Werko, L, Dresdale, D T, Cournand, A, and Richards, D W: Some Effects of Quinidine Sulfate on the Heart and Circulation in Man, Am Heart J, *36*, 816, 1948
98 Ferrer, M I, and Sokoloff, L Antidiuretic Effect of Morphine and Demerol in Congestive Heart Failure, Am J of Med Sc, *214*, 372, 1947
99. Fink, B R, D'Angelo, C J, and Biloon, S Clinical Study of Shock Following Myocardial Infarction, J A M A, *151*, 1163, 1953
100 Freedom, R V, Berger, L M, Cohen, S, and Selle, W. A: Major Neuropsychiatric Residuals Following Resuscitation from Cardiac Arrest, J A M A, *155*, 107, 1954
101 Fries, E D, Partenope, E. A., Lilienfield, L S, and Rose, J C.: A Clinical Appraisal of Pentapyrrolidinium (M. and B 2050) in Hypertensive Patients, Circulation, *9*, 54, 1954.

102. FRIES, E. D, SCHNAPER, H. W, JOHNSON, R L., and SCHREINER, G E.. Hemodynamic Alterations in Acute Myocardial Infarction, J. Clin. Investigation, *31*, 131, 1952.
103 FRIEDBERG, C. K Diseases of the Heart. W. B Saunders & Co, Phila, 1950, p 240
104. ——— (ibid), p 274
105 ——— (ibid), p 494
106 FRIEDBERG, C K, and HORN, H Acute Myocardial Infarction Not Due to Coronary Artery Occlusion, J A M A, *112*, 1675, 1939
107. FRIEDBERG, C. K Revised Criteria for Diagnosis and Treatment of Subacute Bacterial Endocarditis, Med Clin N A *769*, (May) 1950
108 FRIEDBERG, C K., TAYMOR, R, MINOR, J B., and HALPERN, M Use of Diamox, a Carbonic Anhydrase Inhibitor as Oral Diuretic in Patients with Congestive Heart Failure, New Eng J Med, *248*, 883, 1953
109 FRIEDLANDER, R D, and LEVINE, S A Auricular Fibrillation and Flutter without Evidence of Organic Heart Disease, New England J Med, *211*, 624, 1934
110 FRIEDMAN, M, and BINE, R, JR. Observation Concerning the Influence of Potassium Upon the Action of a Digitalis Glycoside (Lanatoside C), Am J Med Sc, *214*, 633, 1947
111 FRIEND, D G, and CUMMINGS, J F New Antiemetic Drug, J A M A, *153*, 480, 1953
112 GARVIN, C F. Infarction in Heart Disease, Am J M Sc, *203*, 473, 1942
113 GERTLER, M M, and YOHALEM, S B Effect of Atabrine on Auricular Fibrillation and Supraventricular Tachycardia in Man, J Mt Sinai Hosp, *13*, 323, 1947
114 GIORMAN, N J, MATTIS, L R, and STEPHENSON, W. F. Studies on the Antidiuretic Action of Morphine, Science, *117*, 225, 1953
115 GLUCK, J, GOLD, H, GREINER, T, MODELL, W, KWIT, N T, THICKMAN, S, OTTO, H L, and WARSHAW, L. Quinidine Sulfate in Propylene Glycol by Intramuscular Injection in Man, J A M A, *145*, 637, 1951
116 GOLD, H Quinidine in Disorders of the Heart Paul B Hoeber, Inc, New York, 1950
117. ———: (ibid), p. 13
118 GOLD, H, and CATTELL, M Mechanism of Digitalis Action in Abolishing Heart Failure, Arch. Int Med, *65*, 263, 1940
119 GOLDENBERG, M, SERLING, I, EDWARDS, T, and RAPPORT, M. M Chemical Screening Methods for the Diagnosis of Pheochromocytoma. I—Norepinephrine and Epinephrine in Human Urine, Am J. Med, *16*, 310, 1954

120 GOLDENBERG, M, SNYDER, C H, and ARANOW, H, JR New Test for Hypertension Due to Circulating Epinephrine, J A M A *135*, 971, 1947

121. GOLDSTEIN, R., and WOLFF, L Hemorrhagic Pericarditis in Acute Myocardial Infarction Treated with Bishydroxycoumarin, J A M A, *146*, 616 (June 16) 1951

122 GONZALEZ SABATHIE, L On the Intravenous Use of Morphine in the Treatment of Paroxysmal Ventricular Tachycardia, Am Heart J, *33*, 719, 1947

123. GORE, IRA The Question of Traumatic Heart Disease, Ann Int Med, *33*, 865, 1950

124 GORHAM, L W, LESTER, D E, WOLF, A V, and SCHULTZ, H H Relative Importance of Dietary Sodium Chloride and Water Intake in Cardiac Edema, Ann Int Med., *27*, 575, 1947

125 GOSSAGE, A M, and HICKS, J A B On Auricular Fibrillation, Quart J Med, *6*, 435, 1912

126 GREINER, T GOLD, H, CATTELL, M, TRAVELL, J, BAKST, H, RINZLER, S H, BENJAMIN, Z H, WARSHAW, L F, BOBB, A L, KIVIT, N T, MODELL, W, ROTHENDLER, H H, MESSELOFF, C R, and KRAMER, M L A Method for the Evaluation of Effects of Drugs on Cardiac Pain in Patients with Angina of Effort A Study of Khellin (Visammin), Ann J Med, 9, 143, 1950

127 GROSSMAN, J, WESTON, R E, EDELMAN, I S, and LEITER, L Studies on Thiomerin—A Subcutaneously Administrable Mercurial Diuretic, Circulation, *1*, 508, 1950

128 GUBNER, R Augmentation of Mercurial Diuresis by Recumbency, Letter to Editor, J A M A, *137*, 401, 1948

129 HAIMOVICI, H, MOSER, M, and KRAKOWER, H The Effect of Oral 688A on the Blood Pressure and Pulse Rate in Normotensive and Hypertensive Subjects, Proc Soc Exper Biol and Med, *77*, 477, 1951

130 HANSEN, W R, MCCLENDEN, R L, and KINSMAN, J M Auricular Fibrillation, Am Heart J, *44*, 449, 1952

131 HARKEN, D E., and WILLIAMS, A C Foreign Bodies in and in Relation to Thoracic Blood Vessels and Heart, Migratory Foreign Bodies Within Blood Vascular System, Am J Surg, *72*, 80, 1946

132 HARKEN, D E Review of Activities of Thoracic Center for III and IV Hospital Groups, 160th General Hospital, European Theatre of Operations, June 10, 1944 to Jan. 1, 1945, J Thoracic Surg, *15*, 31, 1946

133 HARKEN, D E, ELLIS, L B, WARE, P. F, and NORMAN, L. R The Surgical Treatment of Mitral Stenosis, Valvuloplasty, New England J Med, *239*, 801, 1948

134. HARVEY, R M, FERRER, M I, and COURNAND, H The Treatment of Chronic Cor Pulmonale, Circulation, *7*, 932, 1953
135 HARRISON, T. R. Abuse of Rest as a Therapeutic Measure for Patients with Cardiovascular Disease, J A M A, *125*, 1075, 1944.
136 HAUSNER, E P, SHAFER, C L, CORSON, M, JOHNSON, O T, TRUJILLO, T, and LANGHAM, W Clinical Evaluation of Dicumarinyl Derivatives with a Metabolic Study of the Radioactively Labeled Anticoagulants in Animals, Circ, *3*, 171 1951
137 HECHT, H, KATZ, L. N, PICK, A, PRINZMETAL, M, and ROSENBLUETH, A Nature of Auricular Fibrillation and Flutter A Symposium, Circulation, *7*, 591, 1953
138 HELLERSTEIN, H K, and MARTIN, J W.. Incidence of Thrombo-embolic Lesions Accompanying Myocardial Infarction, Am Heart J, *33*, 443, 1947
139 HENDERSON, Y, and PRINCE, A. The Oxygen Pulse and the Systolic Discharge, Am J of Phys, *25*, 106, 1914
140 HERRMANN, G. R, and HEJTMANCIK, M. R A Clinical and Electrocardiographic Study of Paroxysmal Ventricular Tachycardia and Its Management, Ann Int Med, *28*, 989, 1948
141 ——— Atrial Flutter II, Methods of Treatment, Am Heart J, *41*, 182, 1951
142 HESSE, E. Ueber die Funktionsfahigkeit des Verletz ten und genahten Herzens im Lichte der Danerresultate der Herznaht, Deutsche Ztschr f Chir, *190*, 239, 1925
143 HILDEN, T. On Pathogenesis of Acute Pulmonary Edema, Acta, Med Scand, Supp, *234*, 162, 1949
144 HOCK, G A Pheochromocytoma with Paroxysmal Hypertension, J Urology, *61*, 473, 1949
145 HODGES, H A, and GILMOUR, M T.. Myocardial Contusion Report of a Fatal Case with Autopsy, Ann Int Med, *34*, 248, 1951
146 HOMANS, J Venous Thrombosis in Lower Limbs· Its Relation to Pulmonary Embolism, Am J Surg, *38*, 316, 1937
147. HORN, H, and FINKELSTEIN, L E Arteriosclerosis of Coronary Arteries and Mechanism of their Occlusion, Am Heart J, *19*, 655, 1940
148 HAUSER, H B, CLARK, E J, and STOLZER, B L Comparative Effects of Aspirin, ACTH and Cortisone on the Acute Course of Rheumatic Fever in Young Adult Males, Am J. Med, *16*, 168, 1954
149 HOWARTH, S, MCMICHAEL, J, and SHARPEY-SCHAFER, E P Effects of Venesection in Low Output Heart Failure, Clin. Sc, *6*, 41, 1946
150 HOY, S H, and WOOD, J E, JR. Cation Exchange Resins in the Treatment of Congestive Heart Failure, Ann Int. Med, *33*, 1139, 1950

151. Hufnagel, C A, Harvey, W P, Rabil, P J, and others Surgical Correction of Aortic Insufficiency, Surgery, *35*, 673, 1954
152. Hurwitt, E, and Seidenberg, B Rupture of the Heart during Cardiac Massage Ann Surg, *137*, 115, 1953
153 Inhalation Therapy, J A M A, *144*, 25, 1950
154 Izzo, P A, Stevins, R C, Tomsykoski, A, and Rodriguez, C E Hemopericardium Associated with Anticoagulant Therapy, Arch Int Med, *92*, 350, 1953
155 Jaffe, H L, Master, A M, and Dorrance, W R The Salt Depletion Syndrome Following Mercurial Diuresis in Elderly Persons, Am J Med Sc, *220*, 60, 1950
156 Jaffe, H L Electrocardiographic Changes of Coronary Insufficiency During the Formative Stage of Coronary Occlusion, J Mt Sinai Hosp., *16*, 404, 1950
157 Janton, O H Heidorn, B Soloff, L A, O'Neill, T J E, and Glover, R F The Clinical Determination of Mitral Insufficiency When Associated with Mitral Stenosis, Circulation, *10*, 207, 1954
158 James, D F, Turner, H, and Merrill, J Circulatory and Renal Effects of Aminophyllin in Congestive Heart Failure, Am J Med, *5*, 619, 1948, Ab
159 Janeway, L E, Bedell, G N, and Bateman, R D Problem of Mitral Valve Disease, J A M A, *155*, 231, 1954
160 Johnson, J, and Kirby, C K Prevention and Treatment of Cardiac Arrest, J A M A, *154*, 291, 1954
161 Johnstone, M Cyclopropane Anaesthesia and Ventricular Arrythmias, Brit Heart J *12*, 239, 1950
162 ——— General Anaesthesia and Cardiac Inhibition, Brit Heart J, *13*, 47, 1951
163 Jordan, R A, Scheifley, C H, and Edwards, T F Mural Thrombosis and Arterial Embolism in Mitral Stenosis A Clinico-Pathologic Study of 51 Cases, Circulation, *3*, 363, 1951
164 Joseph, S I, and Rovenstine, E A · Cardiac Arrythmias Prophylaxis and Therapy with Procaine Amide During Cyclopropane Anaesthesia for Thoracic Surgery, J Pharm and Exper Ther, *109*, 19, 1951 ab
165. Katzin, H M, Waller, J B and Blumgart, H L "Cardiac Cirrhosis" of the Liver, Arch Int Med, *64*, 457, 1939
166 Kaufman, R E Immediate Fatalities After Intravenous Mercurial Diuretics. Ann. Int Med, *28*, 1040, 1948.
167 Kaydon, H J, Steele, J M., Mark, L C, and Brodie, B B The Use of Procaine Amide in Cardiac Arrythmias, Circulation, *4*, 13, 1951
168. Keeley, J L Saddle Embolism of the Aorta. Report of Successful Embolectomy, Ann Surg, *128*, 257, 1948

169 KELLY, H G, and BAYLESS, R I S Influence of Heart Rate on Cardiac Output, Lancet, *2*, 1071, 1949
170 KELLY, R T, FRIES, E. D., and HIGGINS, T. F The Effects of Hexamethonium on Certain Manifestations of Congestive Heart Failure Circulation, *7*, 169, 1953.
171 KEYS, A, and VILANTE, A: Cardio-circulatory Effects in Man of Neosynephrine, J. Clin Investigation, *21*, 1, 1942
172 KISCH, B.. Das Vorkommen und der Nachweis von Interpolierten Vorhofextrasystolen (Zugleich ein Beitrag zur Kenntnis der Partial extrasystolen), Ztschr f d ges Exp Med, *25*, 188, 1921
173 ——— Strophanthin, Brooklyn Medical Press, 1944
174. ———. The Mechanics of Flutter and Fibrillation Cardiologia, *17*, 244, 1950
175 KISSANE, R W, BROOKS, R, and CLARK, T Relation of Supraventricular Paroxysmal Tachycardia to Heart Disease and the Basal Metabolism Rate, Circulation, *1*, 950, 1950
176 KISSANE, R. W, and KOONS, R A Spontaneous Redigitalization Following Rapid Diuresis in Congestive Heart Failure, Tr Am Therap Soc, *39*, 111, 1940
177 KOSSMANN, C. E, and BERGER, A R Auricular Flutter of 11 Years' Duration with Observations on Esophageal Electrocardiograms, Ann Int Med, *15*, 128, 1941
178 KOUNTZ, N B, SMITH, J R, and WRIGHT, S T Observations on the Effect of Tourniquets on Acute Cardiac Crises, Normal Subjects, and Chronic Heart Failure, Am Heart J, *23*, 624, 1942
179 KROOP, I G: The Treatment of Rheumatic Fever even with Large Doses of Cortisone, New York State J Med, *54*, 2699, 1954
180 KULKA, W: Contusion of the Heart, Am Heart J, *38*, 438, 1949
181 LEAF, A, SCHWARTZ, W B, and RELMAN, A S Oral Administration of a Potent Carbonic Anhydrase Inhibitor ("Diamox") I Changes in Electrolyte and Acid Base Balance, New England J Med, *250*, 759, 1954
182. LEEVY, C M, STRAZZA, J A., and JAFFIN, A E Fluids in Congestive Heart Failure, J A M A, *131*, 1120, 1946
183 LEGER, L, and COSTA, M: Repeated Syncopes Connected with Sinus Hypersensitivity Cured by Carotid Sinus Denervation Presse Medicale, *55*, 173, 1947
184 LEVINE, S A Some Harmful Effects of Recumbency in Treatment of Heart Disease, J A.M A, *126*, 80, 1944
185. LEVINE, S A, and LOWN, B. "Armchair" Treatment of Acute Coronary Thrombosis, J A M A, *148*, 1365, 1952.
186 LEVINE, S A: Clinical Heart Disease, W. B Saunders Co, 1945, p 201

187 ——— Oculocardiac Reflex Electrocardiographic Study With Special Reference to Differences Between Right and Left Vagal and Ocular Pressures in Tabetics and Non-tabetics, Arch Int Med, *15*, 758, 1915

188 LEVINE, S A., and STEVENS, W B. The Therapeutic Value of Quinidine in Coronary Thrombosis Complicated by Ventricular Tachycardia, Am Heart J, *3*, 253, 1928

189. LEVINSON, D C, EDMEADES, D T, and GRIFFITH, G Dissecting Aneurysm of the Aorta Its Clinical, Electrocardiographic and Laboratory Features, Circulation, *1*, 360, 1950

190 LEWIS, T The Mechanism and Graphic Registration of the Heart Beat Shaw and Sons, Ltd, London, 4th Ed, 1925

191 ——— Observations Upon Disorders of the Heart's Action Heart, 3, 279, 1911–12

192 ——— Lecture on Vasovagal Syncope and Carotid Sinus Mechanism, with Comments on Gower's and Nothnagel's Syndrome, Brit M J, *1*, 873, 1932

193 LINENTHAL, A J, and FREEDBERG, A S Medical Progress Measures Used in the Prevention and Treatment of Cardiac Arrhythmias New Eng J Med, *241*, 570, 1949

194 LOWN, B, WYATT, N F, CROCKER, A T, GOODALL, W T and LEVINE, S A Interrelationship of Digitalis and Potassium in Auricular Tachycardia with Block, Am Heart J, *45*, 589, 1953

195 LOWN, B, SALZBERG, H, ENSELBERG, C D, and WESTON, R E Interrelation Between Potassium Metabolism and Digitalis Toxicity in Heart Failure, Proc Soc Exper Biol and Med *76*, 797, 1951

196 LOWN, B, and LEVINE, S A Current Concepts in Digitalis Therapy, New England J Med, *250*, 771 and 819, 1954

197 LUISADA, A A Pathogenesis of Paroxysmal Pulmonary Edema, Medicine, *19*, 475, 1940

198 LUISADA, A A, GOLDMAN, M A, and WEYL, R Alcohol Vapor by Inhalation in the Treatment of Acute Pulmonary Edema, Circulation *5*, 363, 1952.

199 LUNDY, C J, and MCLELLAN, L L Paroxysmal Ventricular Tachycardia. An Etiological Study with Special Reference to the Type, Ann Int Med, *7*, 812, 1934

200 MACGUIRE, W B, JR Risk of Uremia Due to Sodium Depletion, J A M A, *137*, 1377, 1948.

201. MACLEAN, A R., ALLEN, E V, and MAGATH, T B Orthostatic Tachycardia and Orthostatic Hypotension Defects in Return of Venous Blood to the Heart, Am Heart J, *27*, 145, 1944

202 MADDEN, J. L. Resection of Left Auricular Appendix: A Prophylaxis for Recurrent Arterial Emboli, J A M A, *140*, 769, 1949

203. MALLORY, G K, WHITE, P D, and SALCEDO-SALGAR, J ... of Healing of Myocardial Infarction A Study of the P... Anatomy in 72 cases Am Heart J, *18*, 647, 1939
204 MARK, L C, BERLIN, I, KAYDON, H J, ROVENSTINE, E ... STEELE, J M, and BRODIE, B B The Action of ... Amide on Ventricular Arrhythmias, J Pharm and ... Ther, *98*, 21, 1950
205. MARSHALL, D. S Recognition and Emergency Treatment ... Venous Thrombosis and Its Complications, Med Clin of N A,, Nov 1949
206. MARVIN, H. M. Paroxysmal Ventricular Tachycardia with Alternating Complexes Due to Digitalis Intoxication Am Heart J. *4*, *21*, 1928.
207. MASSELL, B F: ACTH and Cortisone Therapy of Rheumatic Fever and Rheumatic Carditis, New England J Med, *251* 183, 1954
208 MASTER, A M · Effort Trauma, Occupation and Compensation in Heart Disease, Bull New York Acad Med, *17*, 778, 1941
209 MASTER, A M, JAFFE, H L, and DACK, S Relation of Effort and Trauma to Acute Coronary Occlusion, Indus Med, 9, 359, 1940.
210. MASTER, A M, DACK, S, and JAFFE, H L Disturbances in Rate and Rhythm in Acute Coronary Artery Thrombosis Ann Int Med, *11*, 735, 1937
211 ——— Partial and Complete Heart Block in Acute Coronary Artery Occlusion, Am J M Sc *196*, 513, 1938
212 MASTER, A. M, GUBNER, R., DACK, S, and JAFFE, H L Differentiation of Acute Coronary Insufficiency with Myocardial Infarction from Coronary Occlusion, Arch Int Med *67*, 647, 1941
213. MASTER, A M, JAFFE, H L, DACK, S, and GRISHMAN, A Coronary Occlusion, Coronary Insufficiency and Angina Pectoris, Am Heart J *27*, 803, 1944
214 MASTER, A. M, DACK, S, GRISHMAN, A, FIELD, L E. and HORN, H. Acute Coronary Insufficiency An Entity Shock Hemorrhage and Pulmonary Embolism as Factors in its Production, J Mt Sinai Hospital, *14*, 8, 1947.
215 MASTER, A M, and EICHERT, H Functional Paroxysmal Auricular Fibrillation, Am J Med Sc, *211*, 336, 1946
216 MASTER, A. M. Digitoxin Intoxication, J A M A., *137*, 531 1948
217. ——— Treatment of Cardiovascular Emergencies, U S Nav M Bull, 39, 190, 1941.
218 MASTER, A M, JAFFE, H L, and DORRANCE, W R The Treatment of Heart Failure New York State J of Med, *50*, 553, 1950

219. MASTER, A M, and JAFFE, H L Complete Functional Recovery After Coronary Occlusion and Coronary Insufficiency J A M A, *147*, 1721, 1951
220 McCANN, U S, BRUCE, R A, LOVEJOY, E W, JR, YU, P N G, PEARSON, R, EMERSON, E B, ENGEL, G, and KELLY, J J. Tussive Syncope, Arch Int Med, *84*, 845, 1949
221 McCORD, M C, and TAGUCHI, J T A Study of the Effect of Procaine Amide Hydrochloride in Supraventricular Arrhythmias, Circ, *4*, 387, 1951
222 MEANS, J H Dyspnoea, Medicine, *3*, 309, 1924
223. MEILMAN, E, and KRAYER, O Clinical Studies on Veratrum Alkaloids, I The Action of Protoveratrine and Veratridine in Hypertension Circulation, *1*, 204, 1950
224 MERRILL, A J Edema and Decreased Renal Blood Flow in Patients with Chronic Congestive Heart Failure Evidence of "Forward Failure" as the Primary Cause of Edema J Clin Investigation, *25*, 389, 1946
225 MERRILL, J P, LEVINE, H D, SOMERVILLE, W, and SMITH, S Clinical Recognition and Treatment of Acute Potassium Intoxication, Ann Int Med, *33*, 797 1950
226 MEYER, J M, CORRELL, H L, PETERS, B J, and LINDERT, M C F Anginal Relief with "Paveril Phosphate" Am Pract & Digest Treat, *3*, 379, 1952
227 MILLER, C G, and RIPSTEIN, C B Resuscitation of the Surgical Patient, Canad M A J, *61*, 255, 1949
228 MILLER, H, ZINN, W J, and GRIFFITH, G C Effect of Heparin and Placebo Therapy in Coronary Artery Disease, Circulation, *6*, 479, 1952
229 MILLER, R, HARVEY, W, and FINCH, C Antagonism of Dicoumarol by Vitamin K Preparation New England J Med, *242*, 211, 1950
230 MITCHELL, A M, DEALY, J B, LOWN, B, and LEVINE, S A Further Observation in the Armchair Treatment of Acute Myocardial Infarction, J A M A, *155*, 810, (June 26) 1954
231 MOKOTOFF, R, ROSS, G, and LEITER, L Renal Plasma Flow and Sodium Reabsorption and Excretion in Congestive Heart Failure, J. Clin Investigation, *27*, 1, 1948
232 MOSER, M Medical Therapy of Essential Hypertension University of Maryland Symposium on Hypertension Baltimore, Md, Oct 1953
233. MOSER, M, GREEN, R, ORBISON, J C, and MATTINGLY, T W. Experience with Autonomic Blocking Agents in Hypertension Washington Meetings of the Am. Fed for Clin. Research Nov. 1952
234. MOSER, M, and MATTINGLY, T W.. Evaluation of the Use of Blocking Agents in the Treatment of Essential Hypertension. In Press Post Graduate Medicine.

235. MOSER, M, SHEEHAN, G, and SCHWINGER, H Pheochromocytoma with Calcification Simulating Cholelithiasis, Radiology, *55*, 655, 1950.
236 MOSER, M, PRANDONI, A G, ORBISON, J A, and MATTINGLY, T W Clinical Experience with Sympathetic Blocking Agents in Peripheral Vascular Disease, Ann Int Med, 38 1245, 1953
237. MOSER, M, PORDY, L, CHESKY, K, TAYMOR, R C, and MASTER, A M The Ballistocardiogram in Myocardial Infarction A Study of One Hundred Cases, Circulation, *6*, 402, 1952
238 MURPHY, F. D, COVELL, H and GRILL, J C The Effects of Intravenous Solutions on Patients With and Without Cardiovascular Defects, J A M A, *116*, 104, 1941
239 NABATOFF, R A, RICHMAN, B, and RIVKIN, L M. Resection of Left Auricular Appendage for Recurrent Arterial Embolization, N. Y. State J Med, 1953
240. NAHUM, L H, and HOFF, H E Auricular Fibrillation in Hyperthyroid Patients Produced by Acetyl-B-Methyl Choline Chloride, with Observations on Role of Vagus and Some Exciting Agents in Genesis of Auricular Fibrillation, J A M A *105*, *254*, 1935
241. NATHANSON, M H. Further Observations on Effects of Drugs on Induced Cardiac Standstill Effect of Epinephrine and Related Compounds, Arch Int. Med, *54*, 111, 1934
242. ——— Modification of Vagus Inhibition of Heart by Quinidine, Proc Soc. Exper Biol and Med, *31*, 1234, 1934
243 NATHANSON, M H, ENGELBERG, H, and HERSH, J Cardiovascular Effects of Paredrine, Am Heart J, 24, 153, 1942
244 NATHANSON, M H, and MILLER, H Clinical Observations on a New Epinephrin-like Compound, Methoxamine, Am J Med. Sc, 223, 270, 1952
245 NICKERSON, M, BROWN, H O, and SCOTT, M Mechanism and Efficacy of Dibenamine Protection Against Spontaneous Cyclopropane Arrhythmias in Surgical Patients, Am J Med, *6*, 396, 1949
246 NUDELMAN, P L, LEFF, I. L, and HOWE, C D. Thrombopenic Purpura Following Quinidine, J A M A, *137*, 1219, 1948
247 OSHER, H. L, KATZ, K H, and WAGNER, D J Khellin in the Treatment of Angina Pectoris, New England J Med, *244*, 315, 1951
248 PAINE, R and SMITH, J R: The Mechanism of Heart Failure, Am. J Med, *6*, 84, 1949
249 PARKINSON, J, and CAMPBELL, M: The Quinidine Treatment of Auricular Fibrillation, Quart J. Med, 22, 281, 1929
250 PALMER, J H, and RAMSEY, C. G Triethanolamine Trinitrate (Metamine) in Treatment of Angina Pectoris Preliminary Report, Canad M A J, 65, 17 1951

251. PARKINSON, J PAPP, C, and EVANS, W.: The Electrocardiogram of Stokes-Adams Attack, Brit. Heart J, *3*, 171, 1941.
252 PARONS, W H, and PURKS, W K. The Elderly Patient as a Surgical Risk, Arch Surg, *58*, 588, 1949.
253 PARRISH, A E. The Bioassay of Adrenal Corticoids in the Urine of Patients with Congestive Heart Failure, J. Clin Investigation, *28*, 45, 1949
254. PATERSON, J C Relation of Physical Exertion and Emotion to Precipitation of Coronary Thrombi, J A M A, *112*, 895, 1939
255 PEARSON, R S B Sinus Bradycardia with Cardiac Asystole, Brit Heart J, *7*, 85, 1945
256. PERERA, G A and BERLINER, R W Relation of Postural Hemodilution to Paroxysmal Dyspnea, J Clin Investig, *22*, 25, 1943
257 PHILLIPS, E, and LEVINE, S A Auricular Fibrillation Without Other Evidence of Disease, Am J Med, *7*, 478, 1949
258 PLOTZ, M Acute Urinary Retention Following the Use of Mercurials in Heart Disease, Urol and Cutan Rev, *47*, 286, 1943
259 PRANDONI, A, and WRIGHT, I S Anticoagulants Heparin and the Dicoumarin -3-3′ Methylene-bis-(4-hydroxycoumarin), Bull New York Acad Med, *18*, 443, 1942
260 PRANDONI, A G, and MOSER, M Clinical Appraisal of Intra-arterial Priscoline Therapy in the Management of Peripheral Arterial Diseases Circulation 9, 73, 1954
261 PRINZMETAL, M, CORDAY, E, OBLATH, R W, BRILL, I C and KRUGER, H E The Nature of Auricular Flutter in Man, Proc Am Heart Assn, June, 1950
262 PRINZMETAL, M, CORDAY, E, BRILL, I C, SELLERS, A L, OBLATH, R W, FLEIG, W A, and KRUGER, H E Mechanism of the Auricular Arrhythmias, Circulation, *1*, 241, 1950
263 PRINZMETAL, M and KENNAMER, R Emergency Treatment of Cardiac Arrhythmias, J A M A, *154*, 1049, 1954
264 RAVITCH, M M and BLALOCK, N. Aspiration of Blood from Pericardium in Treatment of Acute Cardiac Tamponade After Injury Further Experience with Report of Cases, Arch of Surg, *58*, 463, 1949
265 RESENO, W S Thiouracil in Angina Pectoris, Am J Med, *1*, 607, 1946
266. RICE, T B: Low-Sodium Diet, Philadelphia, Lea & Febiger, 1951
267. RICHARDS, D W, JR Dynamics of Congestive Heart Failure, Am J Med, *6*, 772, 1949
268 ——— Cardiac Output by the Catheterization Technique in Various Clinical Conditions, Federation Proc, *4*, 215, 1945
269 ROBERTS, B., SCHNABEL, T G, and RAVDIN, I S: Multiple Episodes of Cardiac Arrest, J A M A, *154*, 581, 1954

270 ROBY, W. H Visual Disturbances with Digitalis Medication New England J Med, *213*, 248, 1935
271 ROSENBERG, J, and DAVIDSON, A G Cough Syncope, N Y State J Med, *54*, 2488 1954
272 ROTH, G. M, and KVALE, W F Tentative Test for Pheochromocytoma, Am J M Sc *210*, 653, 1945
273 RUSSEK, H L., URBACH, K F, DOERNER, A A, and ZOHMAN B L. Choice of a Coronary Vasodilator Drug in Clinical Practice, J A M A, *153*, 208, 1953
274 RUSSEK, H L, ZOHMAN, B L, DOERNER, A A RUSSEK, A S, and WHITE, L G. Indications for Dicumarol in Acute Myocardial Infarction, Circulation *5*, 707, 1952
275 RUSSEK, H L, NAEGELE, C F., and REGAN, F D Alcohol in the Treatment of Angina Pectoris, J A M A *143*, 315, 1950
276 SAMPSON, J J, and SINGER, I M Plasma and Blood Infusions Following Myocardial Infarction, Am Heart J, *38*, 54 1949.
277 SAMPSON, J J, and ZIPSER, A Norephinephrin in Shock Following Myocardial Infarction Circulation, *9*, 38, 1954
278 SARNOFF, S J, GOODALE, W T, and SARNOFF, L C. Graded Reduction of Arterial Pressure in Man by Means of a Thiophanium Derivative (Ro 2-2222), Circulation, *6*, 63, 1952
279 SAYER, W, MOSER, M, and MATTINGLY, T W Pheochromocytoma and the Abnormal Electrocardiogram, Am Heart. J, *48*, 42, 1954
280 SCARRONE, L A, BECK, D F, and WRIGHT, I S Comparative Evaluation of Tromexan and Dicumarol in the Treatment of Thromboembolic Conditions, Circulation, *6*, 489, 1952
281. SCHERF, D., ROMANO, F J, and TERRANOVA, R. Experimental Studies on Auricular Flutter and Auricular Fibrillation, Am Heart J, *36*, 241, 1948
282 SCHERF, D Clinical Progress Treatment of Cardiac Arrhythmias, Circulation, *8*, 756, 1953.
283 SCHLICTER, J G, HELLERSTEIN, H. K, and KATZ, L. N. Factors Involved in Formation and Management of Aneurysm of Heart Regional Meeting, Am. Coll. Phys, Chicago, Nov 1952
284 SCHNITKER, M A, and LEVINE, S A Presence of Digitalis in Body Fluids of Digitalized Patients, Arch. Int. Med, *60*, 240 1937
285 SCHNUR, S., Mortality and Other Studies Questioning the Evidence for and Value of Routine Anticoagulant Therapy in Acute Myocardial Infarction, Circulation, *7*, 855, 1953.
286 SCHWARTZ, S P, and BLOON, S Clinical Signs of Occluding Thrombi of Left Auricle, Am Heart J, *7*, 84, 1931
287 SCHWARTZ, S. P, and DESOLA POOL, N. Transient Ventricular Fibrillation, Am Heart J *39*, 361, 1950.

288 SCHWARTZ, S P, and LEVY, J: Digitalis Studies on Children with Heart Disease, Effects of Digitalis on Edema of Children with Rheumatic Fever and Chronic Valvular Heart Disease in Presence of Sinus Rhythm, Am J Dis Child, *42*, 1349, 1931

289 SCHWARTZ, W B, and LEVINE, S A Case of Paroxysmal Auricular Tachycardia With Block Present Almost Continuously for Twenty-five Years, Circulation, *1*, 936, 1950

290 SCHWARTZ, W B, and RELMAN, A S Electrolyte Disturbances in Congestive Heart Failure, J A M A, *154*, 1237, 1954

291 SCOTT, N M and MOSER, M Potassium in the Treatment of Cardiac Arrhythmias Due to Digitalis Intoxication, Armed Forces Medical J, 5, 511, 1954

292 SCOTT, R W, and SANCETTA, S U Dissecting Aneurysm of Aorta With Hemorrhagic Infarction of the Spinal Cord and Complete Paraplegia, Am Heart J, *38*, 747, 1949

293 SIEGAL, S and HORN, H Quinidine Allergy, Am Heart J, *39*, 302, 1950

294 SIGLER, L H Hyperactive Cardioinhibitory Carotid Sinus Reflex A Possible Aid in the Diagnosis of Coronary Disease, Arch Int Med, *67*, 177 1941

295 SIMON, A J, DOLGIN, M, SOLWAY, A J L HIRSCHMANN, J, and KATZ, L N A Re-evaluation of Papaverine in the Treatment of Angina Pectoris, J Lab and Clin Med *34*, 992, 1949

296 SOKOLOW, M, and EDGAR, A L Blood Quinidine Concentrations as a Guide in the Treatment of Cardiac Arrhythmias, Circulation, *1*, 576, 1950

297 SOLOFF, L A, *et al* Reactivation of Rheumatic Fever Following Mitral Commissurotomy, Circulation, *8*, 481, 1953

298 SPINGARN, C L, and HITZIG, W M Orthostatic Circulatory Insufficiency, Its Occurrence in Tabes Dorsalis and Addison's Disease, Arch Int Med, *69*, 23, 1942

299 SPRAGUE, H B, and WHITE, P D Auricular Flutter Report of a Case of Five Years' Duration with Spontaneous Restoration of Normal Rhythm, J A M A, *90*, 1772, 1928

300 STARLING, E H Some Points in the Pathology of Heart Disease, Lancet, *1*, 569, 1897

301 STARR, I, JR Acetyl-B-Methylcholine—Further Studies of its Action in Paroxysmal Tachycardia and in Certain Other Disturbances of Cardiac Rhythm, Am J. Med Sc, *191*, 210, 1936

302 STEAD, E A, JR The Role of the Cardiac Output in the Mechanism of Congestive Heart Failure, Am J Med, *6*, 232, 1949

303. STEAD, E A, WARREN, J V., and BRANNON, E S Cardiac Output in Congestive Heart Failure An Analysis of the Reasons for the Lack of Close Correlation Between the Symptoms of Heart Failure and the Resting Cardiac Output, Am Heart J, 35, 529, 1948

304 STEAD, E A · Relation of the Cardiac Output to the Symptoms and Signs of Congestive Heart Failure, Mod Concepts Cardiovas. Dis, *16*, No 12, 1947

305 STEAD, E A, and EBERT, R V Postural Hypotension A Disease of the Sympathetic Nervous System, Arch Int Med, *67*, 546, 1941.

306 STEARNS, N S, and ELLIS, L B Acute Effects of Intravenous Administation of a Preparation of Veratrum Viride in Patients with Severe Forms of Hypertensive Disease, New England J Med, *246*, 397, 1952

307 STEMPIEN, S J, and KATZ, K H Quinidine and Potassium in the Treatment of Refractory Paroxysmal Ventricular Tachycardia, Am Heart J, *24*, 555 1942

308 STEWART, C F, and TURNER, K B Note on Pericardial Involvement in Coronary Thrombosis, Am Heart J, *15*, 232, 1938

309 STEWART, H J, DEITICH, J E, CRANE, N F, and THOMPSON, W B Studies of the Circulation in the Presence of Abnormal Cardiac Rhythms Associated with Rapid Ventricular Rate and Rhythms Associated with Slow Ventricular Rate, J Clin Investigation *17*, 449, 1938

310 SWETLOW, G I Paravertebral Alcohol Block in Cardiac Pain, Am Heart J, *1*, 393, 1926

311 TANDOWSKY, R M, OYSTER, J M, and SILVERGLADE, A The Combined Use of Lanatoside C and Quinidine Sulfate in the Abolition of Established Auricular Flutter, Am Heart J, *32*, 617, 1946

312 TAYLOR, D R and POTASHNICK, R Quinidine Induced Exfoliative Dermatitis J A M A, *145*, 641, 1951

313 THOMPSON, S A, and RAISBECK, M J Cardio-pericardiopexy Surgical Treatment of Coronary Arterial Disease by Establishment of Adhesive Pericarditis, Ann Int Med, *16*, 495, 1942

314 THOMPSON, S A Treatment of Angina Pectoris by Surgical Production of Adhesive Pericarditis Am Pract, 3, 31, 1948

315 TOLKOFF, A S W and ADELMAN, M H Resuscitation After Forty Minutes of Cardiac Arrest, J A M A, *139*, 844, 1949

316 URICCHIO, J F and CALENDA, D G The Failure of Hypertonic Saline in the Treatment of Hyponatremia and Edema in Congestive Heart Failure, Ann Int Med, *39*, 1288, 1953

317 TULLOCH, J, and WRIGHT I S Long Term Anticoagulant Therapy Circulation 9 823, 1954

318 VAN DER VEER, B Treatment of Acute Cardiovascular Conditions Med Clin of N A, Nov 1949

319 Van Der Veer, J B, Funk, E H, Boyer, F R, and Keller, E A Clinical Evaluation of Ethyl Bis-Coumacetate (Tromexan), Am J Med, *14*, 694, 1953
320 Vineberg, A Internal Mammary Artery Implant in the Treatment of Angina Pectoris, Canad, M A J, *70*, 367, 1954
321 Waldman, S, and Pelner, L Action of Neostigmine in Supraventricular Tachycardias, Ann Int Med, *29*, 53, 1948
322 Wallach, J B, Lukash, L, and Angrist, A A An Interpretation of the Incidence of Mural Thrombi in the Left Auricle and Appendage with Particular Reference to Mitral Commissurotomy, Am Heart J., *45*, 252, 1953.
323 Walsh, B J, and Sprague, H B Treatment of Congestive Failure in Children with Active Rheumatic Fever, J A M A, *116*, 560 1941
324 Warburg, E J Subacute and Chronic Pericardial and Myocardial Lesions Due to Non-penetrating Traumatic Injuries, Oxford University Press, London, 1938
325 Warren, J V, Brannon, E S, Stead, E A, Jr, and Merrill, A J Pericardial Tamponade from Stab Wound of Heart and Pericardial Effusion of Empyema, Study Utilizing Method of Right Heart Catheterization, Am. Heart J, *31*, 418, 1946
326 Weiner, M, Simson, G, Burns, J J, Steele, J M, and Brodie, B B The Control of Prothrombin Activity with Tromexan Therapy, Am J Med *14*, 689, 1953
327 Weinstein, L and Shelokov, A Cardiovascular Manifestations in Acute Poliomyelitis, New England J Med, *244*, 281 1951
328 Weisberger, A S, and Feil, H Lanatoside C in the Treatment of Persistent Paroxysmal Auricular Tachycardia, Am Heart J, *34*, 871, 1947
329 Weisman, S A Review and Evaluation of Quinidine Therapy for Auricular Fibrillation, J A M A, *152*, 496, 1953
330 Weiss, S, and Sprague, H B Vagal Reflex Irritability and Treatment of Paroxysmal Auricular Tachycardia with Ipecac, Am J Med Sc, *194*, 53, 1937
331 Weiss, S, Capps, R B, Ferris, E B, Jr, and Munro, D Syncope and Convulsions Due to a Hyperactive Carotid Sinus Reflex, Arch Int Med, *58*, 407, 1936
332 Weston, R E, Escher, D J W, Grossman, J, and Leiter, L Mechanisms Contributing to Unresponsiveness to Mercurial Diuretics in Congestive Heart Failure, J. Clin Investigation, *31*, 901, 1952
333. White, P. D Heart Disease, New York, Macmillan Co, 3rd Ed, p 908, 1944
334. White, J C, and Bland, E F Surgical Relief of Severe Angina Pectoris, Methods Employed and End Results in 83 Patients, Medicine, *27*, 1, 1948

335 WILLIAMS, C, and ELLIS, L B Ventricular [illegible]
An Analysis of 36 Cases, Arch Int Med, 71 [illegible]

336 WILSON, M. G, and HELPER, H N Effect of Pit[illegible]
ocorticotropic Hormone (ACTH) in Acute Rheuma[illegible]
J A M A., 145, 133, 1951

337. WISHART, J H, and CHAPMAN, C B Dicoumarol [illegible]
in Congestive Heart Failure, New England J Med [illegible]
701, 1948

338 WOLFF, L. Clinical Aspects of Paroxysmal Rapid Heart [illegible]
New England J. Med, 226, 640, 1942

339 WOLFF, H. G. Life Stress and Cardiovascular Disorder [illegible]
culation, 1, 187, 1950.

340 WOLFF, W. I Cardiac Resuscitation, Complete Recover
After Over Six Minutes of True Circulatory Arrest J A M A
144, 738, 1950

341. WRIGHT, I S, MARPLE, C D, and BECK D F Anticoagu
lant Therapy of Coronary Thrombosis With Myocardial In
farction, J A M A, 138, 1074, 1948

342 WYCKOFF, J., and GOLDRING, W Intravenous Injection of
Ouabain in Man, Arch Int Med, 39, 488, 1927

343 YOUMENS, W. B., GOODMAN, M J, and GOULD, J Neosyneph
rine in Treatment of Paroxysmal Supraventricular Tachycardia
Am Heart J, 37, 359, 1949

344. YOUNG, D, and RODSTEIN, M Results of Cortisone—Cortico
tropin Therapy in Chronic Active Rheumatic Fever, Arch
Int. Med, 90, 64, 1952

345 ZEMAN, F D, and SIEGAL, S Monoplegia Following Carotid
Sinus Pressures in the Aged, Am J Med Sc, 213, 603, 1947

346 ZOLL, P. M, LINETHAL, A J, and NORMAN, L R Treatment
of Stokes-Adams Disease by External Electric Stimulation of
the Heart, Circulation, 9, 482 1954

INDEX

Bold face numbers indicate principal reference

N

Q

R